APR 1 1930

VOLUME 14 NUMBER 1

Medical Lib.

ENDOCRINOLOGY

THE BULLETIN OF THE ASSOCIATION
FOR THE STUDY OF

INTERNAL SECRETIONS

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JANUARY-FEBRUARY

1930

PUBLISHED BI-MONTHLY BY THE ASSOCIATION FOR THE STUDY OF INTERNAL SECRETIONS, SUITE 1214 WILSHIRE MEDICAL BLDG., LOS ANGELES, CALIFORNIA
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THE BULLETIN OF THE ASSOCIATION FOR THE STUDY OF

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Volume 14, Number 1 JANUARY-FEBRUARY, 1930 Serial No. 69

MORPHOLOGICAL CHANGES IN THE ENDOCRINE GLANDS IN MONGOLIAN IDIOCY WITH REPORT OF TWO CASES

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The etiology of mongolian idiocy is as much a mooted point today as it was when the condition was originally described by Langdon-Down (1). The possibility of an endocrine genesis has been the subject of much investigation and discussion, especially with reference to disturbance of the thyroid gland and, to a lesser extent, of the pituitary. This relationship has been suggested on the basis of both clinical association with symptoms referable to dysfunction of the thyroid, numerous examples of which are in the literature (2), and of histo-pathological alteration in these glands as demonstrated on the autopsy table.

The literature on mongolian idiocy as a whole is voluminous but that portion dealing with reports of post-mortem examination of the endocrine glands is comparatively scant. As with most endocrine problems at the present time, the findings have given rise to contradictory interpretations.

Siegert (3) made an intensive study of the literature in 1910 and reported that in the majority of instances normal findings were found on both macroscopical and microscopical examination. He personally feels, however, that in the majority of cases of mongolian idiocy there is at certain times a disturbance of function of the thyroid gland independent of the presence of demonstrable manifestations of hypothyroidism or athyrosis. Kassowitz (4) is also of the opinion that all cases of mongolianism show at times thyroid changes.

Hill (5) reviewed 20 post-mortem examinations of the thyroid gland in mongolian idiocy in the literature and found that morbid changes were noted in several instances as manifested by sclerosis of the gland and degeneration of the colloid substance. He concluded that as yet there is no evidence that any alteration in either the structure or function of the thyroid can be held responsible for this type of idiocy.

According to Wieland (6), the majority of investigators found that the thyroid gland was normal both on microscopic and macroscopic exam-

ination while a small number noted hypoplasia and definite histological changes. The inconstancy of this hypoplastic condition together with the difference in the clinical and anatomical findings in mongolianism and myxedema make him feel that there is no thyrogenetic etiology in this type of idiocy. The occurrance of changes in the thyroid gland and the beneficial results of treatment on isolated symptoms permit the possibility of thyroid alteration in some cases of mongolian idiocy but not in all as claimed by Siegert and Kassowitz.

Thomas and Delhougne (7) observed morphological changes in the thyroid gland of three mongolian idiots. An embryonic type with few follicles and poor colloid content was found in the gland of a 3½ months infant. The thyroid from a 21-months-old infant showed some areas rich in colloid and others of the embryonal type with poor colloid substance. In the gland of the third infant, 8½ months of age, the follicles were abundant but were still of undifferentiated tissue and poor in colloid content. The authors consider that these findings may be normal, as the embryonic state may still be present at this age.

Fromm (8) found on post-mortem examination of an 18-months-old mongolian idiot that the thyroid gland showed a development which was insufficient for the age of that child. There was definite hypoplasia and advanced sclerosis as evidenced by an imperfect development of the glandular substance and a deficiency of the colloid substance as compared with an abundant connective tissue.

Brudzinski (9) also reports a thyroid in a rudimentary state in his patient. A partially sclerosed and atrophied thyroid was found by Bernheim-Karrer (10).

Pathological conditions in the thyroid glands of two mongolian idiots were observed by Bourneville (11). "In the first case, the larger and medium vesicles were much more reduced in number, the lobules were less stretched out, the trabeculae were much hypertrophied and the vessels sclerosed. Here and there were interstitial hemorrhages, a little pigment and fatty infiltration. The capsule was uniformly thickened. There were modifications of the thyroid tissue which, though slight, were still pathological. In the second case, the thyroid gland showed alterations in all its elements. In all the vesicles the colloid material was almost completely replaced by cells derived from glanduar epithelium. The vesicles were completley choked with these cells. Here and there were numerous vesicles filled with fat. The trabeculae were thickened and infiltrated with young connective tissue. There was extensive sclerosis of the thyroid gland" (Hill's translation) (5). In other cases, Bourneville did not find any abnormal changes.

Phillipe and Oberthur (12) observed slight interstitial proliferation about the capillaries, small hemorrhagic areas and some pigmentation of the connective tissue. Lang (13) reported the presence of colloid degeneration of the thyroid gland with interstitial proliferation in his patient.

In Hill's own cases (5), the thyroid and thymus glands were both apparently normal on gross inspection but sclerosis of the thyroid was found on microscopic examination. This was evidenced by a diminution in the number and size of the vesicles, though they were lined by regular cuboidal epithelium and filled with colloid material which stained well. The interstitial tissue was much increased with much round cell infiltration.

In his text book on Pathology, Kaufman (14) states that he personally never observed any pathological changes in the thyroid gland in mongolian idiocy. Meltzer (15) reports that post-mortem examination of the thyroid glands of four mongolians failed to reveal any pathological findings in any of the glands of internal secretion. Likewise a normal thyroid has been reported by Comby (16), Thiemich (17), Chartier (18), Tilloy (19), Cozzolino (20) and Sutherland (21).

There are very few instances in the literature where complete histological descriptions of the other endocrine glands are given. When mentioned, it is generally stated that they were normal. Hill (5), in his review of 20 cases in the literature, reports that the thymus was always found to be normal. Specific mention of a normal thymus is also made by Comby (16), Thiemich (17), Tilloy (19), Chartier (18), Sutherland (21) and Lang (13).

The only instance of abnormal changes in the suprarenal gland is that reported by Lang (13), who observed what he considered to be necrotic changes. These were evidenced by atrophy of the cell bodies and granular degeneration of the protoplasm; the cells were imperfectly separated from one another and the protoplasm showed diminished receptivity to the stain.

With this inconstancy in the finding of pathological alteration in the endocrine glands in mongolian idiocy, it seems timely to report the histopathological pictures observed in two mongolian idiots. It is of interest to note that not only was the thyroid gland affected in each patient but the other glands were the seat of definite pathological changes.

Case 1: M. F., a female infant, 14 months of age, was born at full term by normal delivery and was the only child of young parents who were not related by consanguinity. She presented a typical picture of an associated mongolian idiocy and childhood myxedema as manifested by a small round head, oblique palpebral fissure and superciliary margin with epicanthus, macroglossus, marked hypotonicity of all the muscles, wide open fontanelle, dry skin and hair, cold extremities, incurving of the little finger, large toe separated from the remaining toe by greater distance than normally (prehensile toe). There was a physical and mental delinquency as evidenced by absence of teeth, delay in sitting, inability to walk as yet and no attempt at speech. She has always run a subnormal temperature and had always been constipated. Examination of the eye fundi at the age of seven months revealed normal findings. Roentgenographic examination of the sella turcica at that time showed a small flat type of Class C (Gordon and Bell Classification) (22), within normal limits and shape. The infant had been under my observation at the Endocrine Clinic of the Long Island College Hospital since the age of six months and had been under thyroid and pituitary treatment.

The child was referred by her family physician on Aug. 11, 1928, to the United Israel Zion Hospital with a diagnosis of bronchopneumonia. On admission she presented a typical bronchopneumonia with the usual clinical signs and roentgenographic findings. Blood examination revealed the following picture: Red blood cells, 4,140,000; white blood cells, 7,480; polymorphonuclears, 72; and

lymphocytes, 28. The hemoglobin was 65 per cent (Sahli). The Wassermann and Pirquet tests were negative. She ran a long protracted course characterized by moderate temperature and marked asthenia, finally culminating in death on Sept. 12, 1928.

An autopsy confirmed the diagnosis of bronchopneumonia. On general inspection, all the glands of internal secretion appeared normal with the exception of the thyroid, which was small and firm.

A microscopic study by Dr. Max A. Goldzieher reveals the following changes in the endocrine glands:

Thyroid: Broad strands of collegenous fibres separate the thyroid tissue into islands of variable size and shape; some of the islands are invaded by connective tissue. The acini are very small and are lined by a single row of low cuboidal epithelia. Many of the acini are collapsed and appear as solid epitheliel structures, while others are slightly distended and appear as small cysts. The colloid content is poor, shows many vacuoles and stains poorly.

Adrenals: There is completed involution of the reticularis, the place of the reticularis being taken up by reticular stroma which incloses wide blood filled sinuses. Most of the cortex is formed by well developed trabecularis, whereas the zona glomerulosa is not distinct. The medulla is poorly developed with but a few groups of medullary cells. This is interpreted as physiological involution of the cortex and hypoplasia of chromaffin portion of the adrenal.

Hypophysis: This gland is very rich in eosinophile cells and seem well vascularized.

Ovary: Shows quite a cellular cortex with a large number of primitive follicles.

Pineal: This gland is of fairly large size and encloses a large cyst in its center, the wall of which is formed by glia tissue. The rest of the pineal is quite cellular, most of the cells being large with either oval or round nuclei and with regular distribution of chromatin granules.

In summary, the anatomical findings in the endocrine glands were: Cirrhosis and signs of dysfunction of thyroid gland; physiological involution of adrenal cortex with hypoplasia of chromaffin substance; pineal normal except for the presence of cyst lined by glia cells; normal pituitary gland and ovary.

Case 2: Florence K., aged 6 weeks, was admitted to the hospital on Dec. 12, 1927, for a congenital pylorospasm which had produced persistent vomiting from birth and which had resulted in an athrepsia accompanied by dehydration. On admission it was noted that in addition she presented a typical picture of mongolianism with slanting eyes, incurving of the little fingers and prehensile toe. The Wassermann reaction was negative. The blood examination showed white blood cells, 16,170; red blood cells, 4,100,000; hemoglobin, 75 per cent. A differential count, according to the Schilling modification, showed: myelocytes, 2; jungling form, 7; stab kernig, 33; segmented, 28; lymphocytes, 20; monocytes, 10.

The post-mortem findings of interest to the present discussion show a thyroid gland which is small and firm on general inspection and a pituitary which is also small and on section shows peculiar striations.

Microscopic examination of the glands by Dr. Max A. Goldzieher reveals the following:

Thyroid: The stroma is considerably increased and bundles of fibres separate the thyroid parenchyma into numerous islands varying in size and shape. Most of the acini are slightly distended and filled with a very thin colloid which stains poorly and is highly vacuolized. The epithelium is of low cuboidal type and forms a single row. Quite a number of the acini are collapsed and appear as solid epithelial structures.

Adrenals: The reticularis is in an advanced stage of involution. It is practically substituted by a loose reticulum which encloses blood filled capillaries. There is also iron pigment present denoting previous hemorrhage. The cortex proper shows a fairly large distinct glomerular layer and a markedly developed trabecularis. In the neighborhood of capillaries are seen a few islands of medullary cells.

Thymus: The physiological structure of the gland is obscured, as no cortical layer is present. The individual lobules are separated by broad septa of loose connective tissue. Dark lymphocyte-like nuclei permeate the entire lobule irregularly and here and there form larger discrete groups which are separated by much paler medullary cells. The Hassel bodies are very numerous and stand together in groups. The smaller ones consist of concentrically grouped cells of

medullary type while the larger ones show central necrosis, some even appear as small cysts filled with detritus.

Pineal: Small, very cellular, and the pineal cells show almost without exception a normal vesicular nucleus. The nuclei of the glia cells are scant.

Pituitary: The gland cells of the anterior lobe are rather small, particularly in the periphery. The capillaries between the gland cells are rather wide, sinus-like and lined by conspicuous reticulum fibrils and cells. Occasionally there is a homogeneous faintly staining substance around the capillary separating the latter from gland cells. The gland cells are better maintained in the center of the organ; there the eosinophiles are conspicuous while the basophiles are absent. A small cyst filled with colloid separates the anterior from the posterior lobe. The latter consists of dense nervous tissue with few nuclei.

In summary the findings in the endocrine glands were: Cirrhosis and dysfunction of the thyroid gland; physiological involution of the adrenal cortex and hypoplasia of the chromaffin portion; retrogressive change in Hassel's corpuscles with an increase in number and hypoplasia of the thymus cortex; incipient atrophy of the anterior lobe of the pituitary gland; normal pineal.

SUMMARY

The histo-pathological changes in the endocrine glands of two mongolian idiots are reported. In the first, 14 months of age, the changes consisted of cirrhosis and dysfunction of the thyroid gland, physiological involution of the adrenal cortex with hypoplasia of the chromaffin substance, a normal pineal except for the presence of a cyst lined by glia cells and normal pituitary and ovary.

The second, 6 weeks of age, presented the following changes: Cirrhosis and dysfunction of the thyroid gland, physiological involution of the adrenal cortex and hypoplasia of the chromaffin portion, retrogressive changes in Hassel's bodies with an increase in number, hypoplasia of thymus cortex, incipient atrophy of the anterior lobe of the pituitary gland and a normal pineal.

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SEDIMENTATION OF ERYTHROCYTES IN THE ENDOCRINOPATHIES

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In contrast with its use in other diseases the red cell sedimentation test has been but little used in the study of endocrine disorders.

Westergren (1) believes that the thyroid exerts positive influence upon the sedimentation velocity of the erythrocytes. D'Abundo (2) has studied the sedimentation time in dementia praecox patients treated with certain endocrine preparations, and obtained contradictory results. Scuderi (3), using this reaction in different patients, obtained a very rapid sedimentation velocity in a patient with Addison's disease. A very important work is that of Vasaturo (4). He has investigated the sedimentation time in thyroidectomized, parathyroidectomized, thyroparathyroidectomized and castrated dogs and also in clinical hyperthyroidism, hypothyroidism and hypogenitalism. Some of the animals operated upon have been treated with the corresponding endocrine preparations and also the patients with hypothyroidism. From his studies he believes that the hypothyroid patients and the animals without thyroids had a slow sedimentation time accelerated by endocrine therapy. The sedimentation time is also rapid in hyperthyroid subjects. In the parathyroidectomized animals there was observed an augmentation of the velocity and also in a small degree in those animals that were thyroparathyroidectomized. The rate found in castrated dogs and in patients with hypogenitalism showed that the male gonads have no influence upon sedimentation time.

Uyeno (5) found nearly always an accelerated sedimentation time in rabbits fed with thyroid and this seemed to be intensified in accordance with the grade of thyrotoxicosis produced. But he observed a similar acceleration in thyroidectomized rabbits. In simple goiter the sedimentation time is slow, augmenting if the patients are treated with thyroid extract.

Recently, Kafka (6) maintained that while, in the infectious diseases and intoxications, the erythrocyte sedimentation and the viscosity of the plasma agree with each other, in all endocrine diseases the sedimentation time is accelerated and the viscosity diminished.

We have investigated this reaction in different endocrinopathies following the technic of Westergren (7). We use a pipette made by Leitz's house. It was 2.5 mm. calibrated and divided into two hundred millimeters, as far as the highest zero mark which shows the cubic centimeter. The blood is taken from the vein at the elbow with a record syringe. Ex-

amination was made of 2 cc. containing 0.4 cc. of a 3.8 per cent solution of sodium citrate, making the withdrawal without venous compression. The blood was discharged into a tube and then transferred to the special pipette which was supported in a vertical position.

The height of the red cell column was read at the end of one hour, of two hours and in some cases at the twenty-fourth hour. In general we believe that the reaction is definite in the second hour, for we have observed that in certain cases the fall is more rapid in the first hour and then becomes slower. The distances recorded at the end of one hour and of the second hour permits expression of the sedimentation velocity by the following formula:

$$\text{S. V.} = \frac{a \div \frac{1}{2}b}{2}$$

in which a represents the first height and b the second.

Since the digestive process hastens the sedimentation time the blood for test is collected before breakfast. Uniquely positive results have been noted in Addison's disease. Last year one of us presented a note, in the "Real Academia de Medicina" (8), on the results obtained in twelve cases and subsequently published a report with the detailed clinical histories and the rate of the erythrocyte sedimentation of twenty-four cases (9). In all these the velocity was rapid, having a special diagnostic interest in its constant acceleration in very atypical clinical cases.

The importance of studying the erythrocyte sedimentation in Addison's disease is seen if one takes into consideration the fact that in the clinic Addison's disease is difficult to diagnose, as one of us has persistently repeated (10), (11), and that the other laboratory data (hypoglycemia, hypocholesteremia, etc.) are very inconstant. The blood sugar curve after a glucose meal at times is of the high type though the initial level may be low, as has been noted in some of our cases.

As is well known, in the subjects with hypoadrenalism several causes (infections, intoxications, traumas, surgical intervention, insulin injections or vaccines) are able to cause severe accidents, even sudden death. From this one deduces, as we said in a recent conference (12), the great desirability of early recognition of adrenal deficiency in all patients, whether these are to undergo operative or the medical treatment already mentioned. This permits one to take all necessary precautions for avoiding mishaps and to avoid the employment of medicaments that may be contraindicated. Marañon (12) recommends in these cases the systematic study of the blood sugar and we believe that it would be useful to determine systematically the sedimentation velocity.

From the study of our cases we believe that the more grave is the adrenal involvement the more rapid is the sedimentation velocity. The velocity test, therefore, has considerable prognostic value and permits us

to balance to a certain degree this laboratory datum with the clinical data of the account of the arterial tension.

In this manner we see that in secondary Addison's disease (14), always less grave, the arterial tension is maintained for some time at the characteristic levels of primary adrenal insufficiency, and the erythrocyte sedimentation takes place also less rapidly. In these secondary cases the principal lesion occurs in the cortex and this makes one think that the acceleration of the sedimentation velocity is principally due to disturbances of the medulla.

We do not know the mechanism for producing this phenomena in the patients with Addison's disease. Our first thought is that it is due to a tubercular condition which is the underlying cause of the disorder in a great many of the Addison's disease cases. But in two of our own cases it was proved at autopsy that the adrenals were invaded by a sclerotic process without active focus in the chromaffin tissue nor in any other part of the organism. We could not discover them either by clinical observation or radioscopy in the other patients.

More recently Morros Sardá and one of us (15) has studied the blood chemistry in two epileptics before and after the extirpation of one adrenal gland, an operation which, as is well known, has been recommended principally by Fisher to combat the convulsions. The sedimentation velocity which before operation was three and two millimeters, respectively, had increased, after twenty-five days, to 46.2 and 59. This observation is of great interest as bearing out the diagnostic value of our sign and showing that it bears a direct relationship with the adrenal incretion without any necessary relationship to the tubercular process as such.

Pico, Franceschi and Negrete (16) have studied in horses the influence of insulin upon erythrocyte sedimentation without obtaining any positive results. But they have noted that in these animals in which the blood sugar was low before the injection of insulin, the sedimentation velocity was always accelerated. In many of our Addisonians the rapid sedimentation coincided with a normal or somewhat elevated blood sugar level, and in other patients with other and different diseases tested in this respect no relationship between the two data could be detected.

In some of these simultaneous investigations of the sedimentation velocity and the blood sugar level before and half an hour after the injection of 30 units of insulin it was found that variations in the sugar level had no influence on the sedimentation velocity.

Recently, Nitzescu and Missir (17) have studied sedimentation velocity in dogs before and after extirpation of the whole pancreas and have noted that it is more rapid after the operation, more or less in accordance with the degree of gravity of the diabetes thus produced. From all these observations it seems evident that the hypoglycemia in Addison's disease is not the factor which leads to acceleration of the sedimentation velocity.

According to Kürten (18), the relation of lecithemia and cholesteremia plays an important part in the erythtrocyte sedimentation, since on this relation depends the ionic permeability of the cellular membrane, the water content of the plasma and the electric capacity and resistance of the erythrocytes; he believes that the sedimentation velocity is the more rapid the greater the cholesterin content of the blood. This conception is not in accordance with the investigations of Salomon, De Potter and Valtis (19) nor our own observations because in many of our patients with Addison's disease the blood cholesterin level was low.

The results obtained in other endocrinopathies are set forth in the following table.

Name	Diagnosis	Basal Metabolism	Sedimentation Velocity
J. B.	Hyperthyroidism	+50	6.75
E. J.	Hyperthyroidism (reactional to pyelitis)	+30	5.00
M. M.	Hyperthyroidism	+60	19.00
E. L.	Hyperthyroidism	+45	18.00
J. S.	Hyperthyroidism	+28	6.00
S. V.	Hyperthyroidism	+67	4.5
M. L.	Hyperthyroidism	+40	2.40
F. S.	Hyperthyroidism	+82	21.50
N. H.	Juvenile goiter with light thyroid reaction	+12	9.00
A. P.	Hyperthyroidism	+32	10.25
M. F.	Hyperthyroidism	+18	6.00
C. S.	Hyperthyroidism	+51	13.75
A. R.	Hyperthyroidism	+39	12.70
B. A.	Goiter with hyperthyroid reaction	+15	2.15
M. N.	Myxedema	—45	15.9
T. E.	Myxedematous infantilism	—30	9.5
L. S.	Myxedema	—50	91.5
M. D.	Acromegaly	....	14.20
A. L.	Acromegaly	....	37.00
V. P.	Hypophyseal tumor, Froehlich's Syndrome	....	3.10
J. S.	Hypophyseal tumor, Froehlich's Syndrome	....	44.00
F. C.	Hypophyseal tumor with genital atrophy. Gerodermia syndrome without adiposity	....	3.00
M. B.	Diabetes insipidus	....	12.50
A. S.	Diabetes insipidus	....	17.50
Z. P.	Hypophyseal dwarfism	....	21.00
F. P.	Geroderma	....	20.37
	After graft	....	26.50
A. D.	Puberal intersexuality of adipose type	—18	3.87
V. Z.	Eunuchoidism	....	28.25
A. B.	Macrogenitosomia	....	16.00
J. U.	Ovarian insufficiency	....	42.00
Y. V.	Ovarian insufficiency	....	57.50
R. P.	Ovarian insufficiency	....	3.00
H. O.	Ovarian insufficiency	....	23.00
M. V.	Ovarian insufficiency	....	12.50
A. L.	Ovarian insufficiency	....	4.20

From the perusal of this table it is seen that in 14 cases of hyperthyroidism the rates were rather slow, but otherwise normal (a finding which is contrary to that of Vasaturo and Uyeno) without regard to the intensity of the clinical manifestations nor of the existing basal metabolic rate. Of three myxedematous subjects two had normal and one had an extraordinarily accelerated velocity. In our hypophyseal cases we found the sedimentation velocity normal in one acromegalic and somewhat rapid in another. Of the three cases of hypophyseal tumor with hypofunctional symptoms a slower velocity was found in two and a more rapid in one. In two cases of diabetes insipidus the velocity was normal. In one case of dwarfism the rate was somewhat rapid. In the cases of genital dis-

turbance (gerodermia, eunuchoidism, intersexuality, macrogenitosomia) the velocity findings are completely contradictory. It is worthy of note in the case of gerodermia in which we investigated the sedimentation velocity before and after graft of testicular substance, according to the procedure of Voronoff, the procedure made no difference.

From our investigations we deduce consequently that the thyroid, hypophysis and the genital glands have no important influence on the sedimentation velocity and, with the exception of Addison's disease, the sedimentation velocity is without diagnostic value in the endocrinopathies.

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THE EFFECT OF CASTRATION ON THE PROLIFERATIVE ACTIVITY AND STRUCTURE OF THE THYROID GLAND IN GUINEA PIGS

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The object of this investigation is to determine if extirpation of the ovaries has any definite effect on the structure and especially on the proliferative activity of the thyroid gland. For this purpose the thyroid gland of the guinea pig was used, for it has been studied previously in a series of investigations by Loeb (1) and his associates, Gray (2), Rabinovitch (3), and McCordock (4). These authors used two methods for determining the effect of various factors on the thyroid gland. In the first place, Loeb (5), in experiments begun in 1919, used the intensity of compensatory hypertrophy which follows extirpation of three-fourths or more of this organ, as a convenient indicator of the activity of the gland. In the second place, Loeb, Gray, McCordock and Rabinovitch made use of the normal gland and here attempted a quantitative measurement of the effect of various factors on the thyroid gland by studying in a quantitative manner the number of mitoses in the acini together with the changes in the size of the acini, of the acinus cells, of the consistency of the colloid and of the number of phagocytes.

The first one of these two methods, namely, the determination of the degree of compensatory hypertrophy, was also employed more recently by Furuya (6), who used, however, the rat for his experiments in which he determined the influence of castration on the intensity of compensatory hypertrophy. This author found that in four female rats which had been castrated compensatory hypertrophy was more pronounced than in two non-castrated female rats. Furuya did not make a microscopical study of the gland but he merely compared the weights of the remaining lobes after extirpation of one lobe of the thyroid gland. Furthermore, he did not compare the structural differences in the normal and castrated animals. It is evident that the relatively slight differences in weight found under those conditions might be greatly influenced by secondary conditions as, for instance, the amount of blood retained in the gland or the amount of adherent fat tissue or the quantity of colloid within the acini. There is also the probability that the two lobes of the gland are not in every case equal in weight.

In our experiments we used the guinea pig, the behavior of whose thyroid was well known through the previous studies mentioned above.

Both ovaries were removed in fourteen animals under ether anesthesia. At varying periods from 14 to 323 days after the operation the animals were killed with chloroform, the thyroids removed immediately and fixed in Zenker's fluid. One or both lobes of the thyroid gland in each case were cut serially. Nine animals were used as controls. Their thyroids were likewise cut into serial sections, either one lobe or both lobes being used in the various experiments. The two groups of animals were kept under as nearly identical conditions as possible. The control animals were killed at the same time as the castrated animals and the thyroid glands were fixed and stained by the same methods.

The proliferative activity in each gland was determined by counting the mitoses in every tenth section in accordance with the previous work from this laboratory. In addition, in studying the sections, the size of the acini, the character of the acinus cells and the condition of the colloid and, in particular, also that of the phagocytic cells in the colloid were compared. The results were as follows:

The average number of mitoses in 14 castrated animals was 245 per gland. But if we exclude in this series the count in guinea pig 393, which seems, for some unknown reason, to be exceptionally high, then the average count is only 186 mitoses per gland including two lobes but omitting the isthmus. A summary of the mitotic counts and of the changes in weight which may influence the mitotic activity in the castrated animals is given in Table I.

TABLE I

CASTRATED GUINEA PIGS

No. of Guinea Pig	No. Days Between Castration and Removal of Thyroid	Mitoses*	Original Weight in Grams	Final Weight in Grams	Gain or Loss of Weight in Grams
314A	14	156	315	380	+65
317	14	49	525	503	—22
390	22	246	423	460	+37
315A	28	414	300	365	+65
920	28	254	485	510	+25
13	42	51	550	525	—25
14	42	51	575	563	—12
392	43	226	?	?	?
744	49	182	500	?	?
393	56	1024	320	420	+100
316A	61	122	330	535	+205
919	69	96	345	480	+135
317A	90	182	355	675	+320
1000	323	384	?	925	?
Average	63	245	418	528	+81

*Mitoses, per whole gland, excluding isthmus.

None of these animals was in heat.

In the control animals the average number of mitoses was 203 per gland. It is unnecessary to give here a description of the normal guinea pig thyroid because it corresponds very closely to that given by McCordock (4). The average number of mitoses per gland in the castrated animals does not deviate very widely from that of the controls. As a matter of fact they can be considered of the same order and within the range of the experimental error.

Evidently there is an increase in the number of mitoses which runs parallel with the increase in the weight of the animal during the period of the experiments, and which is also found in the case of the controls. This confirms the previous observations of Loeb (1) and Rabinovitch (3).

The weight of the castrated animals varied between 300 grams and 925 grams; the average weight was about 470 grams. If we exclude the one older animal weighing 925 grams, then the average weight of the group would be about 455 grams.

The weight of the control animals ranged between 165 and 555 grams; the average weight for this group was about 400 grams. The weights and number of mitoses per gland for the control animals will be found in Table II.

TABLE II

CONTROL GUINEA PIGS

No. of Guinea Pig	Mitoses	Original Weight in Grams	Final Weight in Grams	Gain or Loss of Weight in Grams	In Heat or Not
x	122	?	?	?	No
11	40	500	440	—60	No
12	30	550	555	+5	No
240A	546	255	314	+59	Yes
327A	362	315	525	+210	Yes
231A	140	225	230	+5	No
329A	528	165	275	+110	Yes
97	38	?	480	?	No
920A	22	?	495	?	No
Average	203	335	414	+55	....

In this table an interesting feature is noticeable, namely, that the animals which were in heat at the time of removal and fixation of the thyroid gland for microscopical examination show a much larger number of mitoses in the total gland than the animals that were not in heat at the time of examination. However, at present we consider this finding merely as suggestive and it is intended to confirm this observation in additional experiments.

Again it is noticeable that the decrease in the weight of the animal coincides with the decrease in the proliferative activity of the gland.

DISCUSSION

There does not seem to be any definite relationship between the number of mitoses and the number of days which elapse between the time of castration and the removal of the thyroid gland for purposes of examination. There occurred, however, a few exceptional cases. Guinea pig 393 shows 1024 mitoses for the whole gland; this number seems to be unusually large for the series. No explanation appears to be available for this finding.

Guinea pig No. 1000, examined 323 days after castration, needs especial mention in this series. In this animal the acini were larger than in any other guinea pig of the series. The colloid was hard and considerably retracted from the walls of the acini. The epithelial cells of the acini were flattened in this gland. This flattening was apparently due to pressure exerted from within the acinus cavity by the colloid. There were scarcely any phagocytes noticeable. We are justified in assuming that these changes were caused by the advancing age of the animal because several other older guinea pigs examined especially from this point of view showed a similar structure of the thyroid gland. For the most part, there is no marked difference in the size and character of the epithelium and of the acini between the control and castrated female guinea pigs, although noticeable variations are present in individual cases even in the control animals as mentioned by Gray and Loeb (2).

Furuya (6) experimenting with rats and dogs removed one-half of the thyroid gland and weighed it. In four female rats he removed the ovaries at the same time, and kept the other two as controls. He castrated one female pup and kept the other one as a control. Thirty-two days after the operation he killed these animals and weighed the remaining piece of the thyroid gland. He found that this remaining half of the gland had increased in weight in the castrated female rats 30 to 50 per cent more than in the controls.

This difference may be caused by a number of factors, as stated in the early part of this paper.

Several years ago, Dr. Julius Elson carried out some experiments in this laboratory in which he tested the effect of castration on compensatory hypertrophy of the thyroid gland in guinea pigs. His work is not complete and remains unpublished, but as far as it went there was no definite effect of castration noticeable on the hypertrophic changes found in the thyroid gland.

SUMMARY

Castration in female guinea pigs causes neither any appreciable change in the proliferative activity nor in the structural characteristics of the thyroid gland.

The structure of the thyroid gland of the guinea pig seems to show a tendency toward an increase in the amount of colloid and toward a flattening of the acinar epithelium with advancing age.

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THE OCCURRENCE OF YEASTS IN PATIENTS WITH THYROID DISEASE

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The types of thyroid disease indicated by the title of this paper are exophthalmic goiter, colloid goiter, adenomata, and myxedema.

For four and one-half years I have been investigating patients with lesions of the skin due to fungi. As there is no known method of permanently curing the condition, it seemed obvious that there must be some continued source of contamination. The gastric contents and stools were cultured to ascertain if the intestinal tract was the focus of continual contamination. These cultures were positive on either the first or second trial in every instance. The gastric contents yielded more abundant cultures in many instances than the stools. As many of the patients had annoying sensations in the mouth, the saliva was cultured. The saliva was positive for yeasts in all instances where the cutaneous condition was at all marked. When the saliva was negative, the gastric contents or stools, or both, were positive. The saliva cultures offer a ready method of investigation. The organisms in many instances were grown in various types of sugar solutions. All of the organisms produced alcohol from the fermentable sugars.

The next step in such a study is to determine if the organisms produce the same types of poisons in the body of the patient as in the test tube. The urine of the patients was tested for alcohol and other products of yeast metabolism by the bichromate and iodoform methods (1). The tests were positive in every patient. The degree of positiveness has no relationship to the specific gravity, nor to the acidity of the urine. The acidity of the urine is, however, directly related to fermentative activities in the intestine. These tests are not positive in the urine of patients if fermentation by yeast is not taking place. The use of the tests makes it unnecessary, except for statistical purposes, to culture the various sections of the gastro-intestinal tract.

The bichromate and iodoform tests are utilized for the group of alcohols resulting from yeast metabolism (2). Besides alcohols, aldehydes, and other undetermined substances are formed, which cause reduction. There are many acids formed, which are apparently non-reducing to bichromate. The most common type of alcohol produced is ethyl. The odor of acetaldehyde in the bichromate test shows that ethyl alcohol is excreted unoxidized in the urine, and is oxidized in the test. In some instances there is no odor of acetaldehydes. The quantities of amyl, propyl, and butyl alcohols produced by yeasts are much less than that of ethyl. The amount of any type in the body depends on the diet, and the particular

type of organism present. Attempts to isolate the different types of alcohol in the urine offer some possibility of securing helpful information, but the quantities that might be present are so small that the task would require much effort. The practical application of the search is not important, as the dietary changes cause considerable variation from meal to meal. The metabolic faculties of a particular yeast from a patient are better determined in an incubator by the use of various types of solutions and solid media.

EXOPHTHALMIC GOITER

Mr. I. S., 39 years of age. Seven months before the patient came for examination, he became very restless, and lost weight rapidly. The heart was rapid, and he felt weak in the thigh muscles. For several months the eyes had been prominent. The patient had always enjoyed good health except for bloating after meals and, at times, pain in the epigastrium. The bowels had always been constipated. He had suffered in the last few months from frontal and occipital headaches. The basal metabolic rate was +79. The urine gave a high test for alcohol and other products of yeast metabolism. The saliva cultures showed every inoculation of the media positive for yeasts. The patient was placed on a special type of diet, which has been developed for the treatment of cutaneous lesions due to fungi, (3) and given Lugol's solution three times each day. At the end of six weeks he had gained twelve pounds. The pulse rate was normal, and the basal metabolic rate was +12. At the end of six months he had gained nineteen pounds. The pulse and metabolic rates were normal. He felt well in every way.

The urine observations have been repeated on two other patients. They were patients of surgeons, and have been treated surgically. The end result in one is not satisfactory, and the other has not been traced.

COLLOID GOITER

Mr. P. H., aged six years. This patient has been under my continuous observation since he was two years of age. He came originally because of a cutaneous condition, which was considered to be eczema. He also had asthma. He suffered from the formation of gas in the intestine, and the mushy stools were usually pale in color. They were very acid in reaction, and contained much gas, but nothing characteristic was found. He had various types of skin tests for foods, and in spite of changing the diet to comply with the indications of the tests, he had no improvement in any of his symptoms. When he was four years of age a small goiter became noticeable. It was smooth and soft. When he was four and one-half years of age his skin began to be coarse, the hair dry, the lips thick, and the eyelids puffy. He was less alert mentally. A basal metabolic rate was —25. He was put on small doses of thyroxin, and the physical evidences of thyroid deficiency disappeared. The metabolic rate became normal. As the myxedematous condition developed the thyroid gland decreased in size. The skin condition showed no change during this period. The saliva was not studied for yeast organisms until February, 1929. It was positive. The urine gave a high reading by the bichromate and iodoform tests.

Four other patients with colloid goiter have been studied. One had ringworm of the chest about five months before the goiter appeared. They all showed the same urine findings, and in the one instance where the saliva was cultured it was positive.

ADENOMATA OF THE THYROID GLAND

Mrs. A. M., aged 63 years. Eleven months before the patient was first seen she noticed that a lump was forming in the midline of the neck. It was firm, and seemed to be increasing slightly in size. For a slightly longer time she had noticed itching over the back of the neck, and in the antecubital spaces. She had suffered for years with a great deal of gas on the bowels, and constipation. In her earlier life she had suffered from attacks of headache, associated with nausea and vomiting. The attacks ceased one year before the onset of the skin and thyroid trouble. There was a small firm tumor in the midline of the neck in the isthmus of the thyroid gland. There were no evidences of

hyperthyroidism. Over the antecubital spaces there were many small papules with fine points, which contained a small quantity of clear liquid. The same condition was on the back of the neck. The saliva was positive for yeasts, and the urine gave a high reading by the bichromate and iodoform tests. The patient was put on the special diet, and in a short period of time the skin had cleared up entirely. The thyroid nodule shows no decrease in size, but is becoming less firm in consistency.

The studies on the urine have been repeated with similar findings in three other cases. It is difficult to find a considerable number of patients with this condition who do not have other diseases.

MYXEDEMA

In two cases, besides the boy reported above, the urine has been examined. It was positive in both instances. In these two cases there were marked cutaneous lesions due to fungi. Both patients had had years of gastro-intestinal trouble characterized by gas formation, and constipation before the onset of the myxedema.

RELATIONSHIP OF YEASTS TO DISEASE

The presence of yeasts in the intestinal tract has been known for a considerable number of years. The relationship to pathologic conditions has been questionable. There seems to have been no one who thought of yeasts in the intestine in terms of alcoholic fermentation. The possibility of alcoholic fermentation taking place in the intestine makes their relationship to various pathologic conditions of man very reasonable. In plants their pathogenicity is associated with this process (4). The relation of alcohols to various types of physical conditions, as well as symptoms, is well known. The manufacture of it in the body must necessarily be associated with marked changes and disturbances. Ethyl and propyl alcohol both boil at less than body temperature, so that their presence in even minute amounts would cause unpleasant sensations in the intestine. One of the usual accompaniments of this type of fermentation is the production of gas. There are some yeasts which do not produce gas. They act as oxidizing agents. Yeasts form some of the highest types of alcohols known, and the physical changes in the body associated with an organism of this type would be much more frank than those associated with the organisms producing the lower types of alcohol. The aldehydes produced by yeasts are powerful reducing agents (5). The end products of yeast metabolism vary with the type of media, and with various concentrations of the media. In man this would apply to the inherent chemical constitution of the individual, as well as to the type of food consumed. An organism might cause in two individuals two different conditions, because all individuals, if they could be analyzed to their chemical finality, would be slightly different.

At present there is no simple, or even complex, accepted method of definitely determining the classifications of yeasts. All of the yeasts studied from goiter patients ferment glucose. They grow in sugar solutions as bottom yeasts. The colonies are white in color on Sabouraud's media, and on beer wort agar. As there is such considerable variation in the physical condition of the cells and of their biologic characteristics with

age and nutritional conditions, it seems better to await future developments before attempting to list specifically many of the yeasts found in patients.

The significance of yeasts in patients is most quickly determined by treating patients with cutaneous lesions caused thereby by dietetic methods. The laboratory and the clinical changes in this group of patients furnishes the criteria for considering similar data in patients without cutaneous lesions as indicative that the pathologic expressions in the latter group are the results of yeast metabolism.

All metabolic processes of yeasts are associated with the formation of enzymes and co-enzymes, which are oxidative and reductive (6). The absorption of these foreign enzymes into the blood stream furnishes the mechanism for a disturbance in these basic reactions in the body. This absorption shows that they could be passed through the placenta of the mother to the child, or even through the milk.

BASIC CHEMICAL DISTURBANCE CAUSED BY GOITER

When a goiter is affecting the body in a somatic way, it expresses itself as a disturbance of oxidation. Iodine when in its proper combination in thyroxin, which is the known important secretion of the thyroid gland, is responsible for about thirty-five per cent of the rate of oxidation processes in the body. The formation of excess amounts of thyroxin, as in adenomata, leads to excessive oxidation. The presumably altered type of secretion that is formed in exophthalmic goiter leads to excessive oxidation, but there are some physical changes produced in the body that do not accompany the events associated with the increased oxidation due to adenomata. In myxedema there is loss of gland tissue, so that there is a decrease of oxidative processes. In colloid goiter there is some alteration in the functional activity of the thyroid cells so that they secrete more colloid material than in the normal. The activity of the cells is apparently less than in the normal, but not sufficiently less to decrease materially oxidative processes generally in the body. There is no reason to believe that the formation of a tumor in the thyroid gland has a cause different from that of tumors elsewhere. Whenever a tumor partakes in the functional activities of the gland in which it is located, it follows the same line of functioning as is typical of the structure in which located.

In studying conditions due to yeasts, it must be borne in mind that their activity depends on enzymes and co-enzymes. All cells come from cells. Enzymes come from enzymes. Like produces like. All enzymatic action is reversible. Two enzymes of like type lead to acceleration of activity, and the reverse. Hypertrophies and atrophies result from such activities, as is well shown in many fungal diseases in plants, vegetables, and trees. The study of such diseases has great comparative value (7), (8), (9).

THE STOMACH INTESTINE AND THE SITE OF GOITER PRODUCTION

The painstaking investigations of McCarrison established definitely that the causal factor of simple goiter is, in some cases, at least, in the intestinal tract (10). The marked gastro-intestinal symptoms of patients with exophthalmic goiter furnish criteria to show that there is some type of irritation in the intestine of such patients. McCarrison showed that goiter could be readily transmitted by fecal contamination. He described spores in the stools of patients, and evidently felt that they came from bacteria. He made no cultures for yeasts. He demonstrated that something associated with food, water, soil, and fecal matter was fundamentally causative of goiter. McCarrison did not consider iodine deficiency to be primarily causative, although he had evidence to show that iodine was in some way important. In the treatment of patients, he obtained equally as good results with the use of thymol, salol, and B-naphthol, as with iodine.

RELATIONSHIP OF IODINE TO GOITER

The place of iodine in goiter therapy and prevention has been well established. The reason has not been determined. Its action is most marked in colloid goiter and exophthalmic goiter. There is still some debate about its use in the treatment of hyperthyroidism due to adenomata, and some suspicion that it will cause adenomatous goiters to become hyperactive. The evidence when finally sifted seems to indicate that it is just as valuable in the treatment of this type of hyperthyroidism as that of exophthalmic goiter, and that it does not lead to hyperactivity of the adenomatous goiter.

The soil of most countries that have long been inhabited have been fertilized by animal and human excrement. In animal excrement yeasts, and other types of fungi, are abundant. In human excrement the same state prevails. McCarrison by careful experiments showed that such filthy habits of fertilizing the soil by groups of people rendered the soil more productive of goiter, because the causal factor in such soils is greater than the quantity of iodine. Pasteur found yeasts, as well as other types of fungi, in the soil at all four seasons of the year. The viability of yeasts is something that receives little consideration. Guilliermond has studied this problem (11). The older the civilization, the greater the prevalence of fungus-caused diseases should be, because of certain customs associated with soil fertilization. The sewage is disposed of into the streams and rivers. Water drains from the soil into the same streams and rivers. The water is studied as to bacterial content, but not as to the presence of yeasts and yeast products. The enzymes and co-enzymes of yeasts are also in the water, so that water may be harmful even after the yeasts are removed by filtration.

Fruit and vegetables are grown on polluted soil, and are thereby contaminated. The careful analysis of the symptoms of patients with yeast-

caused lesions of the skin indicates that eating vegetables that are grown in excrement fertilized soil lead to gastro-intestinal disturbances, essentially as gas production. White potatoes, carrots, cabbage, and turnips have been most frequently associated with development of the untoward signs. Among fruits, strawberries and cantaloupes are the most common offenders. The highly active ferments of lima and kidney beans belong in a different category. Their tendency to form gas in the intestine can be largely controlled by adding a few drops of iodine to the water in which they are cooked or by having the individual take five or six drops of Lugol's solution in milk during the meal.

McCarrison demonstrated that iodine rich soil was antagonistic to the state of the ground, which led to goiter production. The quantity of iodine required to be antagonistic to the septic state of the ground which may result from long periods of fecal contamination is infinitely less than required to prevent yeast multiplication and activity in the test tube or in man. The nutritional status of the soil everywhere and the annual temperature ranges in some localities are of themselves marked deterrents to yeast multiplication. Similar data were collected in water in relation to iodine and goiter production, and showed that the iodine was effective in relation to fecal contamination. After analyzing Marine's work in connection with hyperplastic goiter in artificially reared fish, McCarrison concludes that the iodine relationship is one of insufficiency relative to the living conditions of the fish. Liver and liver extract lead to rapid multiplication of microscopic fungi. The water in the lower tanks becomes increasingly more contaminated by fecal discharges of the fishes in the upper tanks. The same principle applies to man in relation to soil, food, and water.

Iodine rich soil contains 400 parts of iodine to ten million parts of soil. On this type of soil animals confined in dirty cages did not develop goiter. Iodine rich drinking water contains 300 parts of iodine in 100 billion parts of water. The quantity of iodine required in the presence of one-tenth of a Fleischmann's yeast cake in order to inhibit fermentation and multiplication ranges from 36 to 360 parts in 75,000 parts of water.

If yeasts cause goiter, and iodine has a definite place in both its treatment and prevention, iodine must have a basic relationship to the life of yeasts. The question may be settled in a striking fashion. Put a yeast cake into a liter flask that is nearly filled with water containing a quantity of sugar, and incubate the mixture at 37.5° C. until fermentation is active, as shown by the rapidly rising bubbles. At this time add Lugol's solution drop by drop. The fermentative activity becomes less and less until it finally ceases. The reaction is quantitative, and relative to the activity of the yeasts. The variability in the activities of yeasts must not be overlooked. If a series of ten fermentation tubes is arranged, all containing the same quantity of a very active yeast, and sugar in twenty-five cubic

centimeters of water, to which Lugol's solution is added by drops according to the number of the tube, the amount of gas rising into the gas tube will be as a descending staircase from tube one to tube ten. In less active yeasts there may be only fermentation in the first three tubes. In all specimens the fermentation has been active in tube one. The same quantity of yeasts was used each time. The concentration of iodine is 36 to 360 parts to 75,000 parts of water. Exact quantitative measurements of gas produced have no value, because of the difference in activity of different specimens of yeast. All of the other intestinal antiseptics used by McCarrison have a similar action on yeast fermentation. Temperature ranges beyond a certain limit have a similar action. There is no multiplication of the yeasts in the tubes containing enough Lugol's solution to stop fermentation entirely. The quantity of iodine required in man to stop gas production by yeasts in the stomach has been found to be quite variable.

The value of iodine in the soil, and in the treatment and prevention of certain diseases, which are the expression of yeast action in the intestine, is clear. Iodine, in sufficient dosage, is a depressant to cellular activity and multiplication, so that its action is two-fold in the goiterous individual. Iodine in minimal amounts is a stimulant to cellular activity and multiplication. The present investigation may be completed by a cultural study of yeasts in the soil of goiter areas in relation to the iodine content of the soil. I am not in a position to make this investigation.

THE SUCCESS OF LUGOL, THE PHYSICIAN

When studying the life of this physician, I was quite unable to determine why he was so successful (12). He called all of the diseases that he treated scrofula. He treated them all by various combinations of iodine. The reasons for his success become obvious when one is familiar with the great prevalence of yeasts in nature.

SUMMARY

All types of thyroid disease are associated with fermentation by yeasts. Yeasts may be found in all patients when proper cultures are made. The results of iodine and other types of therapy, that are inhibitive in alcoholic fermentation, indicate their presence to be causal factors of the disease with which their presence can be demonstrated. Iodine in proper amounts prevents the excessive multiplication of yeasts in the soil, and thereby lessens food contamination. The presence of large amounts of iodine in food and water would be preventive of goiter in man, and also of myxedema. Present methods of treating thyroid disease are empirical.

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DISTRIBUTION AND PREPARATION OF THE OVARIAN FOLLICULAR HORMONE

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Investigators have shown that the follicular or estrus-inducing hormone occurs in the various component parts of the ovary, in the placenta, and in the circulating and menstrual blood of women. Because of the relatively low yield obtainable from ovaries and the scarcity and high cost of these glands a systematic search was instituted to locate if possible a rich source of the hormone. This was essential in order to place any preparation in the hands of the clinician for use in treatment of the ovarian hypofunctions.

EXPERIMENTAL PROCEDURES

The general method outlined by Allen and Doisy, which consists of a modification of that described by Iscovesco, was employed in obtaining the extracts from the different materials used. These preparations were oil-soluble and were tested in olive oil solution according to the technique described by Allen and Doisy. That is, three injections were administered to spayed rats at 4 hour intervals and vaginal smears taken 36 and 48 hours afterwards. Five rats were placed on each dosage and four out of five must show full cornified spreads for a unit.

A typical example of the procedure followed is given. Fifteen lbs. of sow kidneys were ground and extracted with agitation for four hours

TABLE I

YIELD IN ALLEN-DOISY UNITS FROM DIFFERENT SOURCES

Material	*Yield*
Hog ovaries	100 U. per lb.
Hog liver	36 U. per lb.
Cow pancreas	30 U. per lb.
Cow cotyledons	17 U. per lb.
Hog kidney	13 U. per lb.
Hog muscle	9 U. per lb.
Cow uterus	17 U. per lb.
Cow blood	40 U. per litre
Sow blood	43 U. per litre
Hog posterior pituitary	Less than 1 U. per lb.
Hog anterior pituitary	Less than 1 U. per lb.
Hog thyroids	Less than 1 U. per lb.
Hog spleen	Less than 1 U. per lb.
Cow parathyroids	Less than 1 U. per lb.
Cow thymus	Less than 1 U. per lb.
Steer pancreas	Less than 1 U. per lb.
Steer blood	Less than 1 U. per lb.
Hen's eggs—yolk	Less than 1 U. per lb.
Hen's eggs—white	Less than 1 U. per lb.
Vacuum desiccated commercial ovarian residue	280 U. per lb.

with 95 per cent alcohol. The extract was filtered off and a second extraction made in the same way. The meat was then discarded. The combined filtrates were distilled in vacuo practically to dryness. The residue was shaken up with 1 litre of ether. This was filtered and 2 litres of acetone added. A precipitate of phospholipins separated which was twice extracted with 1 litre of ether and 2 litres of acetone. The combined ether-acetone filtrates were distilled in vacuo to dryness. The residue was redissolved in ether and filtered. The ether was removed from the filtrate and the material taken up in olive oil for test purposes.

From this table it will be seen that there exists a fairly wide distribution in the animal body of this hormone. The significance of its occurrence in liver and pancreas to a greater extent than anywhere else excepting the ovaries is not clear.

PREPARATION OF AQUEOUS SOLUTIONS OF THE HORMONE

Since the injection of oils is frequently accompanied by a type of tumor formation at the site of injection, many attempts were made to render the active principle soluble in water. As a result of these attempts it was found that hydrolysis of the oily residue obtained after removing the ether, as described above, rendered part of the active material soluble in water. This result could be obtained by the use of either acids or alkalies.

Acetic, formic, hydrochloric and sulphuric acids were tried. Acetic acid gave the largest yield in water soluble form. In all cases the technical difficulties of removing the excess acid and then salts was so great that when a sufficient degree of purity had been attained, little was left of the original yield of hormone.

Of the alkalies, sodium hydroxide, potassium hydroxide, barium hydroxide, calcium hydroxide, and sodium carbonate were tried. Normal solutions of these alkalies were used and a comparison made of the yields obtained. After boiling the ether residue for ½ hour the mixture was quickly cooled. The soap was filtered off and the filtrate neutralized to pH 7.5 and again filtered. The filtrate was taken to dryness in vacuo and extracted with 95 per cent alcohol. The alcohol filtrate was concentrated in vacuo to dryness and taken up in water.

Barium hydroxide gave the greatest yield of crude material but when all the barium was finally removed the resultant yield was low. Sodium hydroxide was found to give the best practical results and was finally adopted as a routine reagent.

The question arose whether or not it was necessary to carry out all the steps of the modified Allen-Doisy process to the final ether residue stage before attempting a hydrolysis. Comparative studies were made at the various stages in the above procedure by treating with sodium hydroxide. It was found that the estrus-inducing hormone could be rendered water soluble at any stage if boiled with the alkali. However, in

some cases mechanical difficulties in handling more than offset any advantage gained. The final procedure for processing ovaries is given below.

One hundred pounds of ovaries were ground in a meat chopper and extracted for 4 hours with 50 gals. of 85 per cent alcohol. The liquid was centrifuged off and filtered. The tissue was re-extracted with 40 gals. of 85 per cent alcohol for another 4 hour period. During both extractions a continuous agitation was maintained. The second extract was centrifuged and filtered. The tissue was then discarded. The combined filtrates were concentrated in vacuo at about 25° C. to approximately 3 gals. This was made up to 85 per cent alcohol and the heavy precipitate so obtained was filtered off and discarded. The filtrate was concentrated to dryness and taken up in ether. The ether solution was allowed to stand at 4° C. for 48 hours and filtered at that temperature. The filtrate was taken to dryness. This was hydrolyzed by using 10 L. of N. caustic soda per 400 gms. of residue. The mixture was brought to a boil and maintained at boiling for 15 minutes. It was then rapidly cooled and filtered through acid washed paper. The filtrate was neutralized to pH 7.2-7.4 and filtered. The filtrate was distilled to dryness in vacuo. The sodium chloride so formed was removed by dissolving the hormone in 95 per cent alcohol and filtering. The alcohol filtrate was distilled to dryness and the residue taken up in water. By this procedure approximately 40 units per lb. of ovaries was obtained.

SUMMARY

(1) A study of the occurrence of the estrus-inducing hormone in various animal tissues was made. A fairly wide distribution was found to exist.

(2) A method is described by which the oil-soluble form was rendered water soluble.

(3) A satisfactory procedure is given in detail for the manufacture of the hormone from ovaries.

A NEW SOURCE OF THE OVARIAN FOLLICULAR HORMONE

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Due to the relatively small amounts of the follicular hormone present in the ovary, a rich source which was plentiful and cheap became of great importance if this hormone was to be made available to the medical profession. As reported in the previous paper (1), no other gland was found to contain a large supply. In fact, the circulating blood of an animal was the most concentrated source from which it was obtained.

We found that the fetal fluid of cattle, both amniotic and allantoic, contained large amounts of this estrus-inducing hormone. Further, it can easily be prepared from this material in a water soluble form.

OCCURRENCE IN AMNIOTIC AND ALLANTOIC FLUIDS

The uterus was obtained from a pregnant cow slaughtered for other reasons. The sacs were dissected away from the cotyledons and each sac was pierced separately and the liquid carefully collected. As judged from the fetus the animal was approximately 5 months pregnant. Two thousand one hundred cc. of amniotic fluid and 1100 cc. of allantoic fluid were so obtained. Both fluids were clear and amber-colored. Identical procedures were followed in each case.

They were mixed with alcohol to give a final concentration of 75 per cent and filtered from a light flocculent precipitate. The extract was concentrated to dryness in vacuo. The residue was an alkaline paste which was neutralized with hydrochloric acid and dissolved in water. A clear solution was obtained. The volume of the amniotic concentrate was 61 cc., and that of the allantoic 48 cc.

These were tested upon spayed white rats according to Allen and Doisy's technique without modifications. The amniotic concentrate tested 3 units per cc., or 87 U. per litre, and the allantoic 2 units per cc., or 87 units per litre. Apparently the distribution is approximately the same in both, and hereafter no attempts were made to keep them separate.

EXTRACTION AND PURIFICATION

Various attempts were made at the purification of this hormone from the fetal fluid using all the methods previously tried for the preparation of the hormone from other sources. The best procedure so far obtained is as follows:

Ninety gallons of frozen fetal fluid were melted and mixed with alcohol to give 75 per cent concentration. This was stirred for several hours

and then filtered from a protein precipitate. The clear filtrate was concentrated in vacuo to approximately 5 gallons. This concentrate was made up to 50 per cent alcohol and again filtered from a flocculent precipitate. This filtrate was distilled to a thick paste and extracted with 4 gals. of 90 per cent alcohol. A heavy, dark brown, gummy precipitate settled out. The supernatant liquid was decanted and the residue re-extracted with 2 gallons of 95 per cent alcohol. The extracts were combined and ether added to give a concentration of at least 40 per cent. Another gummy brown precipitate settled out. The alcohol-ether solution was decanted and distilled to dryness. The residue was taken up in 2 litres of 95 per cent alcohol and 4 gallons of ether added. A further precipitation occurred. The filtrate was concentrated to dryness and the residue dissolved in water. A small amount of material is insoluble and this was removed by filtering through hard paper. All distillations were carried out in vacuo. All precipitates were discarded. The yield by this procedure varied from 128 units to 200 units per gallon of fetal fluid.

The product so obtained is of a fair degree of purity and is non-toxic. Analysis of a typical preparation in a 10 unit per cc. dilution showed an amino nitrogen value of 0.45 mgm. per cc.; urea nitrogen, 0.84 mgm. per cc.; total nitrogen, 12.46 mgm. per cc.; phosphorus, .134 mgm. per cc., and an ash of 0.45 per cent. This material showed no loss of potency after heating at 125° F. for 32 days. It produced a very slight transitory fall in blood pressure of a dog under amytal anesthesia.

The water solution of the hormone was crystal clear and yellow brown in color. It was non-toxic. As high as 100 units have been given a rat with no effect except to prolong the estrus phase of the cycle. Six hundred and thirty-eight units were administered to a monkey (Macacus rhesus) weighing 2.3 kgms. over a period of 6 days with no toxic effect. No local irritation was observed.

PHYSIOLOGICAL PROPERTIES

To establish the identity of the estrus inducing substance obtained in this way with the follicular hormone obtained from the ovary, it was felt that at least three other properties should be established, viz., the hastening of sexual maturity in an immature rat, the induction of menstruation in the spayed and immature monkey, and the feminization of a male animal.

INDUCTION OF SEXUAL MATURITY IN IMMATURE RATS

As a control, preparations from ovaries, placenta and fetal fluid which had been previously assayed to determine their estrus inducing properties in the spayed rat were administered to immature rats. Solutions were made up to contain 1 unit in 0.2 cc. Injections were given daily until opening of the vagina occurred.

Cage No.	No. of Rats in Cage	Source	Date of Birth	Av. Age of Rat at date of Opening Days	Remarks
1	4	Controls	1-9-28	51	Injection started
2	5	Fetal Fluid	1-9-28	22.5	1-27-28 and con-
3	5	Ovaries	1-9-28	23	tinued until vagi-
4	5	Placenta	1-9-28	22.5	na opened in all
5	4	Controls	1-13-28	54	except controls.
6	5	Fetal Fluid	1-13-28	18.5	1 unit daily

INDUCTION OF MENSTRUATION IN SPAYED MONKEYS

In another paper (2) we have given in detail the technique and results obtained in the induction of menstruation in both ovariectomized and immature monkeys. In all cases, provided an adequate dosage was administered, menstruation was obtained.

INDUCTION OF A FEMALE CHARACTERISTIC IN A MALE MONKEY

Various authors have reported that the breasts and nipples of male guinea pigs could be induced to grow and the testes and penis to retrogress by the injection of ovarian follicular hormone. In the female Macacus rhesus monkey there is a certain marked secondary characteristic associated with the sexual cycle. The area about the buttocks and extending for several centimeters up the under-side of the tail and down between the legs corresponding to the area occupied by the male scrotum becomes red and swollen during the intermenstrual period, the color and swelling subsiding a few days before menstruation and reappearing a few days after. In the spayed female this same condition may be reproduced by injections of ovarian hormone.

The male Macacus rhesus has no periodic cycle and normally manifests no color or swelling of the sexual skin. By the injection of ovarian hormone we were able to induce a reddening and swelling in a male monkey similar to that which occurs in a female. No change could be detected in the nipples or in the testes and penis although the sexual activity of the animal seemed to be diminished, he having been kept with a female during the course of the experiment. The experiment is summarized in tabular form:

Wt., 5 kg. Experiment started 1-16-29.

Date	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
Units injected...	30	30	30	30		30	30	30	30	30	30		30	30	30
Color of skin...				1			1	1	2	3	3	1	1	2	3
Swelling of skin.							x	x	x	x	x	x	x	x	x

SUMMARY

1. The ovarian follicular hormone has been demonstrated to be present in the fetal fluid of cows in sufficient amounts to warrant its extraction on a commercial scale and a process has been outlined for its extraction and partial purification.

2. The hormone has been shown to be identical with that extracted from ovary in that it will induce estrus in a spayed rat, menstruation in a spayed monkey and in an immature monkey, hasten the opening of the vaginal orifice in an immature rat and has a feminizing action when injected into a male animal.

Work is being done on the further purification of the hormone, and the establishment of certain of its chemical and physiological properties.

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Book Reviews

MODERN METHODS OF TREATMENT. Logan Clendening, 1929. With chapters on Special Subjects by H. C. Anderson, J. B. Cowherd, H. P. Kuhn, Carl O. Richter, F. C. Neff, E. H. Skinner and E. R. DeWeese. The C. V. Mosby Company, St. Louis. Pp. 815.

The book includes a 21-page chapter on the use of endocrine products. This is an interesting practical critique on organotherapy by one who is neither an enthusiast nor a nihilist. It is recognized that in properly selected cases excellent results may be obtained and the reason for the many failures that are obtained are discussed. These, as he says, may follow from any one of five as yet uncontrollable causes: "(1) The symptoms present may be due to a dysfunction of the gland, not to either simple deficiency or to simple superabundance of normal secretion; that is, the gland may be pouring out a strange secretion from any produced in health. (2) The methods of administration of the extracts may not be proper. In some instances oral administration may be totally ineffective. For all we know they should be given intravenously. This is not said here in a critical spirit. It is simply a suggestion, the outcome of thinking about my own failures. The proper method of administration of these extracts is still almost totally outside the field of our present knowledge. (3) The product given may be inert. These extracts deteriorate rapidly. We have no good methods of standardization. (4) The symptoms for which the patient is being dosed may not be the deficiency of the gland, the extract of which is being administered, at all. This mistake in diagnosis may be made, in the odor of sanctity—with the best information on our state of knowledge at present. (5) It may be too late. The bodily changes which have occurred may be fixed and use of the gland cannot cause retrogression—examples of this are treating cretinism after the third or fourth year, or Frölich's syndrome after the fifteenth year."

It is interesting to note that the author has the courage to advocate pluriglandular therapy in pluriglandular disorders.

LOS ESTADOS INTERSEXUALES EN LA ESPECIE HUMANA. G. Marañon, 1929. Javier Morata, Madrid. Pp. 262.

For many years the author has been interested in the morphological and functional aspects of sexuality. In this book he has brought together a great many personal observations and supplemented them with material from the literature—with which, incidentally, he shows a catholic acquaintance. Among the interesting topics treated are the conception of intersexuality; morphological aspects of sexuality; classification of intersexual states, such as hermaphroditism, pseudohermaphroditism, gynecomastia, virilism, masculinism, etc.; theories of sexuality, endocrine factors in sexual processes and possible treatment of the conditions. Chapter XX comprises a resume of the significance of virility and feminity in human evolution and in social problems. The thesis that various glands of intersexuality are of common occurrence is ably defended. It is emphasized that all endocrine deviations have a repercussion in the sexual sphere.

The book is well printed and is illustrated with numerous striking photographs. An excellent bibliography is included. The work is worthy of wide attention.

BODILY CHANGES IN PAIN, HUNGER, FEAR AND RAGE. Walter B. Cannon, 1929. D. Appleton & Company, New York and London. Pp. 404.

The readers of this Journal need no introduction to this well-known classic. In the fourteen years since the publication of the first edition many more pertinent data, nearly all supporting the original thesis, have been published. These have been succinctly included in the new edition.

The book has been amplified by five new chapters on emotional increase of blood corpuscles, emotional derangement of bodily functions, thirst, two on theories of emotion with the presentation of an attractive alternative to the well-known James-Lange theory.

INNERE SEKRETION IHRE PHYSIOLOGIE, PATHOLOGIE UND KLINIK. Julius Bauer, 1927. Julius Springer, Berlin and Wien. Pp. 478.

The subject of endocrinology has become too extensive for detailed treatment in any single volume. The author recognizes this fact and makes no attempt at encyclopedic completeness. The book represents the accumulation and, more important the discarding of years of teaching and clinical experience in this field. It is a book intended to give a judicious survey of the field from the physiological, morphological, pathological and clinical points of view.

The book is clearly written, attractively though not copiously illustrated and well printed. An excellent working bibliography—largely of more recent contributions—is incorporated as a series of foot-notes as in Sharpey-Schafer's well-known book.

The book is worthy of a place among the half dozen best that comes to mind when one desires a general treatment of the subject of the internal secretions.

THE PIGMENTARY EFFECTOR SYSTEM. A REVIEW OF THE PHYSIOLOGY OF COLOUR RESPONSE. T. L. Hogben, Biological Monographs and Manuals (Edit. F. A. Crew and W. Cutler) No. 1. Oliver and Boyd. Edinburgh. 1924.

Reviewed in Endokrinologie, **3**: 239. 1929.

THE ENDOCRINES IN GENERAL MEDICINE. W. Langdon Brown, 1927. Paul B. Hoeber, Inc., New York.

Reviewed in Biol. Absts. **3**: 583. 1929.

GOITER PREVENTION AND THYROID PROTECTION. Israel Bram, 1928. F. A. Davis Company, Philadelphia. Pp. 327.

Bram's book is primarily a popular presentation of his well known thesis that exophthalmic goiter is a constitutional disorder much more amenable to medical than to surgical treatment. As such, it is frankly devoted to a considerable extent to special pleading. Whatever may be

the propriety of addressing the lay public on matters upon which medical opinion is so divergent, the mass effect of the book will no doubt be good. It is an effective tract against the evils of "jazz" living.

One must regret, however, the inclusion of a few extreme or dubious statements. It is sweepingly averred, for instance, that no patient with a ductless gland disturbance can become or remain well as a tobacco habitué. Schiff's old experiments—unwittingly on the parathyroid glands—are cited as evidence of the vicious effect of flesh diet in thyroid disorders. In general, the alleged harmfulness of meat eating is overstressed. The carbon dioxide of popular beverages—a substance with which the human body is at all times charged—is noted as harmful.

The book is entertainingly written and is well printed. The sections on practical management of exophthalmic goiter should be particularly valuable not only to lay, but to many medical readers.

The book includes numerous other features, such as discussions of thyroid biology, varieties of goiter, distribution of endemic goiter and goiter prophylaxis. The chapter on endemic goiter is written by Dr. Robert Olesen.

DISEASES OF THE THYROID GLAND. Arthur E. Hertzler, 1929. With a chapter on Hospital Management of Goiter Patients by Victor E. Chesky. The C. V. Mosby Company, St. Louis. Pp. 286.

One of the most worth while books on diseases of the thyroid is that of Dr. Hertzler, which now appears in a second edition. It is unique among American works in being based on a thirty years' study of a stable community in which many opportunities have been utilized to observe the evolution of individual cases of thyroid disease. The data thus appears in longitudinal rather than cross-sectional perspective. The writer is an independent thinker with the courage of his convictions and a command of picturesque exposition. The book should receive the close attention of those interested in either the biology or the clinical treatment of thyroid disease.

It is attractively printed and beautifully illustrated with photographs and drawings of original material.

DIABETES LATENTE. Felix Puchulu, 1929. Bartolomé Mitre, Buenos Aires. Pp. 213.

Under the direction of and, to some extent, in collaboration with Professor Escudero, the author has made an extensive study of the occurrence, manifestations and treatment of latent diabetes. He speaks for the early recognition of the condition and its treatment under a dietary-insulin régimen before it evolves into a more difficult overt diseases.

The technic evolved in Escudero's clinic for the diagnosis of latent diabetes is described and discussed in relation both to numerous personal cases reported and to the recent literature on the topic.

IODINE IN NUTRITION. A REVIEW OF EXISTING INFORMATION. J. B. Orr and I. Leitch, 1929. London: His Majesty's Stationery Office. Pp. 108.

Reviewed in J. A. M. A. **93**: 871. 1929.

El Metabolism Basal en la Clinica. Con especial aplicacion al diagnostico y tratamiento de las enfermedades de las glandules de secrecion interna y de la nutricion. Mariano R. Castex and Mario Schteingart, 1929. Buenos Aires, Ancieto Lopez. Pp. 239.

Reviewed in J. A. M. A. **93**: 871. 1929.

The Adrenals: Their Physiology, Pathology and Diseases. Max A. Goldzieher, 1929. Macmillan Company, New York. Pp. 436.

Reviewed in J. A. M. A. **92**: 1377. 1929.

Keimdruse, Sexualitat und Nervensystem. O. Kauders. S. Karger, Berlin.

Reviewed in J. Nervous & Mental Disease, **70**: 457. 1929.

Syndrome neuro-hypophysaire. D. Guglielmo, 1928. (Institut d'edit. Scient. de Milan.)

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Vue generale sur l'endcrinologie d'apres 25 ans de pratique. Léopold-Lévi, 1929. Ed. Paul-Martial, Paris.

Reviewed in Rev. franç. d'endocrinol. **7**: 322. 1929.

Endocrine Disorders. Hans Curschmann, 1929. With an introduction by Franz Prange. Oxford University Press, London.

This book is a translation from the German book by the same author, and is designed as a clinical manual based upon a wide personal clinical experience. Within the limited space of 180 pages, the author presents an instructive resumé of the present day practical and theoretical knowledge of the disorders of the glands of internal secretion. The pineal and thymus glands are included in addition to the thyroid, parathyroid, pituitary, adrenals and the gonads. In appendices are described allied conditions, such as mongolian degeneration, dystrophia pigmentosa, myotonia and lipodytrophy. Under diseases of the gonads, Prange gives an interesting and instructive presentation of sexual inversion, hermaphroditism, homosexuality and rejuvenation. The book is well printed, excellently translated and contains numerous photographs from the author's practice.

Physiologie gynecologique et medecine des femmes. H. Vignes, 1929. Ed. Masson et Cie, Paris.

Reviewed in Rev. franç. d'endocrinol. **7**: 321. 1929.

Pneumogastrique, appareil thyroidien et activite cerebrale. D. Santenoise, 1929. Ed. A. Legrand, Paris. Vol. I, pp. 336.

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Le probleme des glandes a secretion interne. Les proprietes physico-chimiques et pharmacodynamiques des hormones. I: L'hypophyse. H. Peneau, L. Blanchard and H. Simonnet, 1929. Les Presses Universitaires de France. Pp. 249.

Reviewed in J. A. M. A. **93**: 1015. 1929.

La Therapeutique par les Glandes (Opotherapie). Louis Moinson, 1928. Le François, Paris. Pp. 191.

Reviewed in J. A. M. A. **93**: 1016. 1929.

Die Hormone Ihre Physiologie und Pharmakologie. Bd. I. Keimdrusen. Hypophyse. Nebennieren. Paul Trendelenburg, 1929. Julius Springer, Berlin. Pp. 351.

Reviewed in J. A. M. A. **93**: 1016. 1929.

Sterilization for Human Betterment. E. S. Gosney and Paul Popenoe. The MacMillan Company, New York, 1929. Pp. 202.

Over 6,000 sterilizations had been performed in the one state of California prior to January 1, 1929, and the authors have traced the records and results of these sterilizations as far as possible. The first part of the book is devoted to a summary of the author's findings, and the second part to some conclusions to which these findings and a general consideration of sterilizations have led. The authors particularly point out that sterilization destroys no organ or gland of the body, and shows no effect upon sex desire, sex performance, or sex feelings of the subject, thus removing some of the principal objections advanced by opponents of this social and economic measure, so long contemplated and now seriously considered.

Thus the book is of technical interest to endocrinologists only in a negative way. The fact that eugenic sterilization can be carried out without interference with hormone production is of such social importance that this negative aspect is worthy of wide dissemination.

Hormone and Stoffwechsel. (Die Bedeutung der Hormone fur der Stoffhaushalt tierischer u. pflanzlicher Organismen.) [Hormones and metabolism.] W. Raab. Naturwissensch, und Landwirtsch. **10**: F. P. Datterer, Freising-München, 1926. Pp. 195.

Reviewed in Biol. Abstracts, **2**: 1590. 1928.

La neurocrinie hypophysaire. Etude histophysiologique du complexe tubero-infundibulo-pituitaire. Remy Collin, 1928. Gaston Doin et Cie., Paris. Pp. 102.

Reviewed in Biol. Abstracts, **2**: 1586. 1928.

Handbuch der Inneren Sekretion. Ed. M. Hirsch. Bd. II, Lief. III. Curt Kabitsch, Leipzig. Pp. 504. Thomas, E., G. Bayer and G. Zuelzer.

"It is a difficult and thankless task to discuss the physiology of an organ about which so little is positively known," writes Dr. E. Thomas as an introduction to his discussion of the thymus gland. He takes as a point of departure the older work claiming an interference with growth and metabolism in dogs when the thymus is extirpated, but missed the classic paper of Park and McClure showing the mythical character of the thymic factor. He agrees, however, that the organ can be extirpated without lasting harm. The evidence of inter-relationships between the thymus, thyroid and sex glands is recognized. While the literature cited is predominantly German, a considerable number of papers in other languages is noted. The article runs to 44 pages.

The next 390 pages comprise a discussion by Professor G. Bayer of the physiology of the adrenals. The treatment of the subject is admirable throughout. It shows wide acquaintance with the literature and keen critical judgment—a quality very necessary in dealing with a subject so replete with contradictions. Space does not permit an analysis of the article in detail. Suffice it to say that anyone desiring a well-balanced, readable discussion of adrenal physiology can profitably turn to this one. The well chosen biblography runs to 33 pages.

Professor G. Zuelzer closes the volume with brief discussions of the endocrine functions of the salivary glands, stomach, intestines, liver and spleen.

HANDBUCH DER INNEREN SEKRETION. Ed. M. Hirsch, Bd. III, Lief. I. Curt Kabitzsch, Leipzig. Pp. 201. Deusch, G., H. Curschmann, E. Wieland and F. Siegert.

Professor G. Deusch treats together, under the caption "Hyperthyroses" the various disorders in which overactivity of the thyroid gland is a prominent feature. While no attempt is made in an article of 70 pages to deal exhaustively with the subject, such outstanding topics as have become classic in such treatises are covered in an interesting way. The literature reviewed is well selected to exemplify the best thought at this time.

Professor Hans Curschmann devotes 27 pages to a discussion of hypothyroidism in adults and 8 pages to an appendix dealing with Chaga's disease and adiposis dolorosa. The section is notably incomplete. The last section is the best.

A creditable and well illustrated article by Dr. E. Weiland of Basel deals with hypothyroidism in children (44 pages) and an equally satisfactory article (53 pages) by Professor F. Siegert sets forth the outstanding knowledge of athyroses in children.

HANDBUCH DER INNEREN SEKRETION. Ed. M. Hirsch. Bd. III, Lief. II. Curt Kabitzsch. Pp. 386. Josefson, A., B. Aschner, E. Thomas, R. Ehrmann, L. Dinkin, O. Herschan, F. C. Geller, A. Hermstein, G. Hirsch and L. Fraenkel.

Dr. A. Josefson of Stockholm discusses somewhat briefly the diagnosis of acromegaly and gigantism, dystrophia adiposo-genitalis and Simmond's disease. A few unenthusiastic remarks on treatment conclude the chapter. The article is notable for its original illustrations. The bibliography is incomplete in content and in form, but is well selected.

In an article of 27 pages, Dr. B. Aschner gives an excellent presentation of what information is available on diseases of the pineal gland. The author demonstrates his command of the world's literature.

Dr. E. Thomas reviews a few of the German papers on clinical aspects of thymus deficiency (9 pages).

One of the notably satisfactory chapters of the series is that of Drs. R. Ehrmann and L. Dinkin on the clinical pathology of the adrenals. Acute and chronic Addison's disease, hyperfunction of the medulla and of the cortex are separately treated. The bibliography is unusally complete and is up to date.

Developmental disorders related to ovarian functions as portrayed in the German literature are discussed by Dr. O. Herschan (40 pages).

From a like point of view, Dr. F. R. Geller treats of sexual and kindred functional disturbances of women (46 pages).

In a similarly narrow way, Dr. A. Hermstein deals with disturbances of pregnancy (47 pages), and Dr. G. Hirsch with the mammary glands in relation to internal secretion (28 pages).

Finally, Professor L. Fraenkel has brought together some unusual German medical lore on the effects of endocrine neoplasms on the genital apparatus. Among the illustrations are four beautifully reproduced in colors (32 pages).

HANDBUCH DER INNEREN SEKRETION. Ed. M. Hirsch. Bd. III, Lief III. Curt Kabitzsch, Leipzig. Pp. 248. Klose, H., G. Büttner and H. Eggenberger.

This volume comprises two chapters on thyroid deficiency. In the first, Drs. Klose and Blüttner discuss the subject of cachexia thyreopriva (strumipriva). The first sections include a historical discussion of the results of thyroid extirpation in men and animals with reproductions of numerous illustrations from the classic contributions, the cause of the disorder and the end results in various organs. The section on results in animals is especially interesting. The numerous other topics that conventionally go to make up a chapter of this kind are in general well treated. An admirable bibliography completes the chapter, though one notes with surprise the absence of any reference to Halsted's work.

Dr. Eggenberger discusses goitre and cretinism at length, utilizing the rich material of Switzerland for illustration, though the goitre belts of the entire world are surveyed. The geographical, morphological and chemical aspects of the goitre problem are well treated, as is the matter of propylaxis. The article is completed in the next succeeding volume of the series. The illustrations are notably good. Spatial limitations do not permit detailed note of all the many excellences of the chapter. It closes with a good bibliography of the world's best contributions.

HANDBUCH DER INNEREN SEKRETION. Ed. M. Hirsch. Bd. III, Lief IV. Curt Kabitzsch, Leipzig. Pp. 445. Eggenberger, H., G. Peritz, E. Leschke and W. Cimbal.

In addition to the closing part of Dr. Eggenberger's chapter on goitre and cretinism previously noticed, this volume includes a 60-page discussion of the parathyroid by Dr. Peritz, one of 164 pages on disturbances of the autonomic nervous system by Dr. Leschke, and one of 102 pages by Dr. Cimbal on endocrine factors in the psychoses and neuroses. The two latter are derived very largely from German sources and are of correspondingly limited authority.

HANDBUCH DER INNEREN SEKRETION. Ed. M. Hirsch. Bd. III, Lief VI. Curt Kabitzsch, Leipzig. Pp. 273. Pulvermacher, L., M. Rosenberg, A. v. Szily, F. Poos and P. Krantz.

The volume is made up of a discussion of the possible endocrine function of the skin by Dr. Pulvermacher, of diabetes by Dr. Rosenberg, of internal secretions and the eye by Drs. v. Szily and Poos, and internal secretions and dentistry by Dr. Krantz. The volume is largely devoid of illustrations and the sources are largely German.

Abstract Department

Adrenalin in malaria. Aguilar, R. Ann. Int. Med. **2**: 1343. 1929.

The author injects 8-15 minims of adrenalin chloride when quinine is administered for pernicious malaria. Nine cases are reported in which this mode of treatment was successful.—E. L.

The suprarenal glands and hypertension: A study of the veins within the suprarenal glands. Allen, E. V., Ann. Int. Med. **3**: 153. 1929.

Veins of the suprarenal gland, the individual areas of the lumens of which in cross sections are between 19.9 and 30.0 sq. mm. have, in cases of hypertension, a ratio of muscle to lumen twice as great as that in cases of normal blood pressure. Theoretically, this hypertrophy indicates the following: (1) increased function of the suprarenal glands, (2) overactivity of the sympathetic nervous system, or (3) the effect of noxious substances in the blood stream. The total area of the lumens of all veins, as defined in the paper, is greater in cases of hypertension than in cases of normal blood pressure. This shows that there is a higher degree of vascularization in the former which probably indicates a higher level of functional activity. These observations are distinct evidence of a close relationship between increased functional activity of the suprarenal glands and hypertension.—Author's Abst.

The clinical symptoms and laboratory data in the diagnosis of Addison's disease (Los síntomas clínicos y los datos del laboratorio en el diagnostico de la enfermedad de Addison). Bonilla, E., Guipúzcoa Médica, No. 141, 43, 1928.

The diagnosis of atypical disease may be very difficult if one regards only the classic symptoms. The author discusses the inconclusiveness of skin pigmentation as well as its typical manifestations. Blood examinations give more significant data. In this disease one generally encounters leucopenia, lymphocytosis, reduced blood sugar and cholestrin and depression of the alkaline reserve. The most valuable single datum is accelerated segmentation time of the red cells. This is found constantly and appears early in the course of the disease.—G. M.

Experiments with adrenaline. Burridge, W. and D. N. Seth, Quart. J. Physiol. **19**: 14. 1929.

This is a report of the effects of adrenaline on the frog heart perfused with low-calcium Ringer solution. It was found that the drug, in all dilutions, was augmentory, but there was also an independent depressing action, the altered contraction height representing a balance betwen two opposing effects. Adrenaline affects acceleration of the change from systole to diastole, apparently by shortening the refractory period and thus giving the depressing effect. The particular results obtained in a given experiment depend on existing conditions at the time, such as the cardiac reserve and the conditions demanding cardiac response.—C. I. R.

Regenerative power of adrenal tissue (Essais de régénération des tissues surrénaux). Celestino da Costa, A., Compt. rend. Soc. de biol. **100**: 517. 1929.

In rabbits one adrenal was removed entire and later most of the remaining gland. Even after two months the portion in situ showed no evidence of regeneration.—J. C. D.

On the adrenalin content of the suprarenal capsules in experimental traumatic shock (Sul contenuto in adrenalina delle capsule surrenali nello shock traumatico sperimentale). Dogliotti, A. M. and G. Giordanengo, Ann. ital. di chir. **8**: 391. 1929.

A fall of blood pressure is a constant and fundamental symptom in the morbid picture of traumatic shock. It is known that increased adrenalin output follows a violent painful stimulus. Also, in the pressure curve of experi-

mental traumatic shock there is observed after a reflex rise a secondary rise in arterial pressure, which continues 15 or 20 minutes. This phenomenon has been interpreted as a consequence of the excessive production of adrenalin in the first period of shock. In suprarenalectomized dogs the pressure curve lacks this secondary rise. This study was undertaken to determine, by means of quantitative determination of the adrenalin content of the suprarenal glands, their behavior in the presence of severe trauma. Insufficiency of the suprarenals consequent to an initial excess of function is suggested as a part of the later picture. Guinea pigs were used. The suprarenal glands were removed, extracted, and the adrenalin content was determined by the method of Battelli, by that of Folin, Cannon and Denis, and by injecting the extracts into a rabbit's jugular vein and measuring the arterial pressure. The extracts of fresh gland and to a less degree the extracts of dried gland from the animals which had undergone the most severe experimental trauma (evisceration, multiple fractures associated with tearing of the sciatic nerves) showed a constant diminution of the adrenalin content, evident one hour after the trauma and of greater degree after 6 to 8 hours. The extracts of the suprarenals from animals undergoing simple tearing of one sciatic or simple fractures of the limbs showed little differences in adrenalin content. The maximum diminution in adrenalin content observed from 6 to 8 hours after the greatest trauma was estimated to be from one-half to one-third of the content of the gland of normal animals. The two methods of estimation used (colorimetric and biological) gave corresponding values.—L. C. Wyman.

Suprarenal apoplexy as the cause of an extensive perirenal haematoma (Apoplexie de la glade surrénale causée par un hématome périrénal étondu). Fedinec, Bratisl. lekár. listy, **9**: 108. 1929.

The author has observed a case of unilateral suprarenal apoplexy. The patient was a badly nourished woman of 35 who, while walking, was attacked suddenly with a violent pain in the right lumbar region, associated with vomiting and persistent sensation of pressure in the right hip. On post mortem hemorrhage into the right suprarenal capsule was found, the cause of which could not be determined by microscopic examination of the organ.

—Author's Abst.

The action of strychnine upon the denervated heart and upon the secretion of adrenalin. Hormon, P. M. and C. M. McFall, J. Pharmacol. & Exper. Therap. **37**: 131. 1929.

In decerebrated cats with denervated heart, but with adrenal and liver innervation intact, strychnine does not directly increase the output of adrenin. Morphine has no effect on the denervated heart if the adrenals are tied off. If the latter are intact, there is a marked and sustained acceleration. It is believed that this is due to increased secretion of adrenin.—C. I. R.

On adrenal pathology (Zur Nebennierenpathologie). Kovacs, W., Beitr. z. path. Anat. u. z. allg. Path. **79**: 213. 1928.

Eight cases showing bilateral lesions of the adrenals are fully reported and discussed chiefly from their pathological and physiological aspects. The classification adopted and the grouping of the cases is as follows: Cytotoxische schrumpfnebenniere, 1 case; vaskuläre schrumpfnebenniere, 3 cases; tuberculosis of the adrenals, accessory adrenals, etc., 4 cases. In the case of simple atrophy the regenerated nodules of cortical tissue suggested a similarity with cirrhosis of the liver. The toxin responsible for the adrenal damage may be endogenous and haematogenous, and the atrophy being bilateral emphasizes this as a possibility. Observations in post mortem and experimental material have shown the cortex to be essential to life while destruction of the medullary chromaffin tissue can be compensated for by hypertrophy of a similar tissue in the sympathetic system. When only the cortex of one gland has been destroyed, compensatory hypertrophy occurs in the surviving gland and no evidence of the Addisonian syndrome results. In one case of the series cortical regeneration was slight and yet the patient survived for a considerable time. Incomplete cortical destruction even if very severe will not result in an acutely fatal termination. Although the cortical lesion may be essential in the production of Addison's disease yet medullary damage must also play a part. But medul-

lary lesions alone are of little significance. On the whole the results of this investigation lead the author to believe that the organ as a whole was involved in Addison's disease. As for the relationship between cortex and medulla interaction is essential as suggested by their vascular supply. The cortex and medulla each have an afferent artery but only the medulla possesses an efferent vein. The cortical blood in passing through the medulla must add its contribution to the medullary secretion before the adrenal product reaches the body generally. For this reason medulla without cortex cannot function effectively.
—William Susman.

Histamine and adrenalin in relation to salivary secretion. Mackay, Margaret E., J. Pharmacol. & Exper. Therap. **37**: 349. 1929.

Histamine did not give a constant effect on salivary secretion in cats and dogs and in those experiments in which there was no response, blood pressure records showed a fall followed by a rise instead of a continuous depressor response. After removal of the adrenals a uniformly increased secretion was obtained and no rise in blood pressure. Continuous slow intravenous injection of dilute adrenalin after removal of the adrenals, was followed by histamine injection with poor secretory response. The results are interpreted as indicating increased secretion of adrenalin after histamine and an antagonism between the two substances.—C. I. R.

On the pathogenesis of serious symptoms of suprarenal insufficiency (Sur la pathogénie des accidents graves de l'insuffisance surrénale). Marañon, G., Presse méd. **63**: 1021. 1929.

This paper presents a discussion of hypoglycemia and of acidosis in suprarenal insufficiency, both from the clinical and from the experimental viewpoint. The author's contributions were based upon the observation of 104 cases of Addison's disease in all its forms, in 15 of which he had been able to make an anatomical and pathological study. The serious symptoms of suprarenal insufficiency may be classed in three groups: sudden death, digestive symptoms which resemble cholera, peritonitis or appendicitis, and nervous symptoms such as psychopathic, meningitic, myoclonic, and convulsive or comatose. A disturbance of carbohydrate metabolism is present in Addison's disease. There may be an actual hypoglycemia or a latent hypoglycemia which may be demonstrated by the use of insulin or by other means. In organisms with spontaneous or experimental suprarenal insufficiency there is a tendency to acidosis. This acidosis is more serious when definite symptoms of the digestive or encephalopathic type appear and develops parallel with these symptoms. This leads to the conclusion that acidosis is important in the pathogenesis of certain of the symptoms of Addison's disease, but does not exclude other factors such as hypoglycemia, hyperviscosity, other intoxications, etc. The acidosis in Addison's disease appears to be concerned with the disturbance of carbohydrate metabolism, which is of a type opposite to that in diabetes. It does not appear to be comparable to nephritic acidosis. After the injection of glucose in cases of Addison's disease symptoms of acidosis appeared. This is in accord with certain experimental work in animals. The exact mechanism of this acidosis is not determined, but certain experimental work indicates that hepatic insufficiency may play a part. There may be hepatic insufficiency in Addison's disease. Antiacidosic treatment is therefor indicated to combat the symptoms mentioned.—L. C. Wyman.

Primary and secondary adrenal insufficiency (Insuficiencia suprarrenal primitiva y secundaria). Marañon, G., Medicina Latina, **1**: 4. 1929. Also Rev. Españ. de med. y. cir. **12**: 11. 1929.

Adrenal insufficiency presents two types with intervening grades that are of interest from the standpoint of both pathogenesis and prognosis, namely, the primary and secondary forms. Many cases of Addison's disease are seen in which there is evidence of an underlying constitutional factor. They show general hypoplasia, tendency to infantilism and to status thymicolymphaticus. This constitution is believed to be a result of congenital adrenal insufficiency, which lowers the resistance to tubercular infection. This constitutional hypoplasia may explain the great frequency of Addisonian manifestations in Spain. The secondary cases are those in which there is no constitutional liability to

infection, the adrenals being involved more or less incidentally. It is interesting to note that in the primary forms melanoderma is likely to appear late and to be slight in degree in comparison with other symptoms; in the secondary types it is likely to appear early and to be intense. The prognosis is much more grave in the primary type.—E. B.

Muscular lactic acid in suprarenalectomized rats (El acido lactico muscular en las ratas suprarrenoprivas). Mazzocco, P., Rev. Soc. argent. de biol. **4**: 1. 1928. Also Compt. rend. Soc. de biol. **99**: 174. 1928.

Rats were attached to a board, the vertebral column was sectioned, and the caudal end of the cut spinal cord was stimulated by means of a faradic current of such a strength that the hind legs were rigid in tetany for one minute. At this point one hind leg was ligated, the muscles extirpated and frozen between two plates of glass. The muscles of the other leg were extirpated after ½, 1, 2, 3 or 4 minutes. Lactic acid was determined by a method similar to those of Meyerhoff and of Embden. The average amount of muscular lactic acid, after tetanization of one minute, was greater in three lots of suprarenalectomized rats than that in three lots of controls. The determinations were made 10, 30 and 60 days after operation. The rate of decline of the amount of lactic acid following the period of tetanization did not bear a regular relation to the time of rest, but in general the recuperation was a little better in the controls than in the suprarenalectomized rats.—L. C. Wyman.

The use of adrenalin in its effect on basal metabolism in the diagnosis of latent hyperthyroidism (Del estudio de los efectos de y en especial al de los hipertiroidismos latentes). Micó. Arch. d'Endocinol. y Nutricion, **2**: 49. 1927.

Injection of a half milligram of adrenalin in normal subjects produces a slight increase in the basal metabolic rate. In hypothyroid subjects it produces a lesser effect or none. In typical hyperthyroidism the basal metabolism although initially high promptly increases more than 30 per cent after the injection of adrenalin. There is a group of cases of latent hyperthyroidism in which the clinical picture is obscure, and the basal metabolism is within normal limits, but in which the injection of adrenalin produces a sudden elevation of the basal rate. This fact is of diagnostic value. This is particularly true of cases in which thinness is the only notable manifestation of the disorder. The reaction permits an easy differentiation between neuroses that give manifestations similar to hyperthyroidism and true latent hyperthyroidism. The reaction is also of value in gauging the treatment of thyroid insufficiency. It discloses the onset of masked therapeutic hyperthyroidism.—E. B.

Effects of intravenous injections of adrenin on tired muscle (Action de l'adrénaline en injection intraveineuse sur les muscles fatigués). deMira, F. and J. Fontes, Compt. rend. Soc. de biol. **101**: 976. 1929.

Injections of dilute solutions of adrenin reduced the fatigue in rabbit muscle. The effects of the injection were prolonged to 45 minutes. The salutary effects of various cortical extracts may be due to very minute traces of adrenin present in them. To test this, very dilute solutions of adrenin were examined for their power to relieve the fatigue in the flexor muscle in the rabbit's foot, tired by electrical stimulation. Dilutions of .0016 mgm. per kilo of body weight were effective, .016 mgm. was most efficient, and doses of .02 mgm. and over were deleterious. The increase in power of contraction was very striking and lasted for more than an hour. The result is ascribed to capillary dilatation.—J. C. D.

The effects in two clinical cases of unilateral extirpation of the adrenal glands (Estudio de la funcion suprarrenal en dos casos de extirpacion unilateral de esta glandula). Morros Sarda, J. and A. Moya Gaston, Med. ibera, **1**: 729. 1928.

Following unilateral extirpation of the adrenal glands from two epileptic subjects the authors noted moderate variations in the blood sugar, blood cholestrin, and alkaline reserve. The most significant change was in the red cell sedimentation time, which was increased respectively from 3 and 2 mm. per hour to 46 and 59. These results confirm the opinion of Bonilla and Moya that this is a valuable diagnostic datum in cases of adrenal insufficiency.—E. B.

Suprarenal cortical extracts in suprarenal insufficiency (Addison's disease). Rogoff, J. M. and G. N. Stewart, J. A. M. A. **92:** 1569. 1929.

The authors report promising results from the use of an adrenal cortex preparation by mouth in 7 cases of adrenal deficiency. The nature of the extract is not disclosed.—R. G. H.

The part played by the adrenal cortex in development of cancer (Rôle du cortex de la surrénale dans le dévelopement du cancer). Sokoloff, B., Compt. rend. Soc. de biol. **101:** 264. 1929.

Marked enlargement of the adrenal gland takes place in chickens suffering from the Rous sarcoma, and a distinct but less striking change in mice with Bashford's carcinoma. The changes in the cortex include dedifferentiation followed by degeneration.—J. C. D.

Studies on suprarenal insufficiency V. The non-protein nitrogen and urea in the blood of suprarenalectomized rats. Wyman, L. C. and B. S. Walker, Am. J. Physiol. **89:** 349. 1929.

Following double suprarenalectomy in rats the non-protein and urea nitrogen of the blood may be increased, the amount of increase tending to parallel the severity of the symptoms of suprarenal insufficiency. Such increases were not noted in rats having either gross accessory cortical tissue or successful cortical transplants, in the absence of demonstrable chromaffin tissue. Following control blank operation infrequent, moderately high values for both substances were found during the first two weeks after operation, but these values were not as high as those observed in suprarenal insufficiency. Otherwise the values obtained were normal. The results indicate that the high values for non-protein and urea nitrogen of the blood observed after suprarenalectomy are associated with cortical insufficiency. It is suggested that this is further evidence for a function of the suprarenal cortex concerned with the steady maintenance of certain bodily conditions.—Authors' Summary.

Studies on suprarenal insufficiency VI. Anaphylaxis in suprarenalectomized rats. Wyman, L. C., Am. J. Physiol. **89:** 356. 1929.

Of a group of 25 doubly suprarenalectomized rats sensitized with horse serum 36 per cent died from anaphylactic shock following the test dose, 20 per cent had severe symptoms, 12 per cent had moderate symptoms, and 32 per cent had slight symptoms. No correlation was found between the presence or absence of gross accessory cortical tissue or the time of survival after operation and the susceptibility to anaphylactic shock. A group of 29 normal rats sensitized with horse serum had, following the test dose, no symptoms or only slight or moderate symptoms. Of 15 of these rats which were suprarenalectomized after the test injection 12 died of anaphylactic shock following a second test dose injected after operation. Of 15 suprarenalectomized rats having autoplastic cortical transplants, and in some cases gross accessories as well, 40 per cent died from anaphylactic shock following sensitization and the injection of a test dose of horse serum. An attempt to reduce the susceptibility of suprarenalectomized rats to anaphylactic shock by means of injections of adrenalin chloride solution gave suggestive though incomplete evidence of possible protection from this source. It is concluded that suprarenalectomized rats are more susceptible than normal rats to anaphylactic shock, and that this increased susceptibility is not related to cortical insufficiency, but that it is consequent to the lack of medullary suprarenal tissue—Author's Summary.

Studies on suprarenal insufficiency VII. Note on temperature regulation in suprarenalectomized rats. Wyman, L. C. and Caroline Tum Suden, Am. J. Physiol. **89:** 362. 1929.

After two hours in a moderately cold room normal rats, suprarenalectomized rats with autoplastic cortical transplants, and suprarenalectomized rats having gross accessory cortical masses (with two exceptions) have similar slight variations in the rectal temperature. All these have no marked external reactions to the cold and recover their original normal temperature after one hour at room temperature following exposure to cold. Rats having cortical

insufficiency show a fall in the rectal temperature after two hours in the cold room, show more or less marked external reactions to the cold, and do not recover their original temperatures in a warm room as soon as those having cortical tissue. The fall of rectal temperature upon exposure to cold and the inability to rapidly recover normal temperature is correlated with the degree of cortical insufficiency which is present. It is concluded that the suprarenal cortex, as well as the medulla, is indirectly concerned with heat regulation.
—Authors' Summary.

Sudden death and glands of internal secretion (Muerte subita y glandulas de secrecion interna). Bonilla, E., Rev. Ib.-Am. de Cienc. med. **3**: 231. 1928.

The author discusses at length the significance of endocrine factors in vulnerability. The article does not lend itself to abstracting.—R. G. H.

Standardization of biological products. Burn, J. H., Internat. Clin. **3**: (Series 39) 15. 1929.

Among other things the author calls attention to the biological assay of insulin, pituitary extract and ovarian hormone. The original definition of the unit of insulin was the amount required to cause the blood sugar of a normal fasting rabbit (weighing 2 kgm.) to fall to the value of 0.045 per cent. Soon it was discovered that this unit was extremely variable. A common standard of reference was therefore called for and the assay of insulin became comparative. The modified procedure now amounted to the examination of an unknown sample and its comparison with the standard to find out how much stronger or weaker the former might be. Until 1928 there was no available proof that the potency of pituitary extract as measured by its oxytocic property on the guinea pig represented its potency for obstetrical purposes. That oxytocin is responsible for contraction of the human uterus has now been proved, while Bourne and Burn have found that vasopressin is devoid of any uterine effect. Recently it was shown that an estimate of the oxytocic property does not offer a trustworthy guide to the amount of pressor and antidiuretic constituents. There is at present no satisfactory animal method of measuring the antidiuretic effect. Experiments on rats have yielded evidence of the potency of ovarian hormone prepared in 1923 by Allen and Doisy. The unit of ovarian hormone was described as the least quantity sufficient to cause oestrus in an ovariectomized rat of 140 gm. weight. This definition was later modified by Coward and Burn, who redefined the unit as the amount of hormone required to produce oestrus in 50 per cent of rats, which made ample allowance for variation of response in experimental animals. The author calls attention to the need, in biological assay, of careful consideration of individual variations in response to the substance assayed, whether it be a matter of laboratory animals or the human patient.—I. B.

Blood sugar studies on children with endocrine dysfunctions, using the author's micro Folin-Wu method of quantitative blood sugar estimation. Byrd, T. L., South. M. J. **22**: 729. 1929.

Blood sugar determinations were made on the following types of endocrine cases: cretins, 4; mixed mongol-cretin, 3; hypothyroid, 1; obesity with hypopituitary, hypothyroid, and hypogonad, 7; anterior pituitary deficiency, 3. Some received treatment while others did not. The results obtained were not constant and could not be related; high tolerance was found with treatment and in the absence of treatment. The author concludes that blood sugar tolerance tests are of no special value in differentiating hypofunctioning endocrine glands. Treatment does not seem to alter the blood sugar content to any great degree.—M. B. G.

Operative treatment for atrophic or poorly developed endocrine glands by implantation of a new arterial circulation. Goljanitzki, I. A. and A. I. Obolenskaja, Arch. f. klin. Chir. **154**: 623. 1929.

The authors believe that treatment of endocrine deficiency by the known methods, viz., organotherapy, homo- and heteroplastic transplantation and ligation of the excretory ducts of mixed glands, fails in such cases as eunuchoidism, infantilism, etc., because these conditions are primarily disorders of the central or sympathetic nervous system or the blood circulation in relation to the

affected glands. The authors have obtained evidence both by animal experimentation and clinically in man that by supplying such atrophied or aplastic glands with a new arterial circulation and a new innervation it is possible to favorably influence or restore function. The sex glands of rabbits, which were cut off from their nutritive circulation were saved from necrosis by the implantation of the spermatic artery into the testis in the male and of the artery of the ligamentum lata into the ovary in the female. A new vessel plexus was observed to have been formed in the place of implantation. The operation with eunuchoids consisted in implanting the proximal stump of the inferior epigastric artery into either the split atrophic testis or the spermatic cord and suturing the lumboinguinal nerve to the spermatic nerve. In a myxedema tuberosum patient a stump of the right lingual artery was implanted into the right lobe of the atrophic thyroid.—N. K. Schaffer.

A new circulatory hormone. Second report (Uber ein neues Kreislaufhormon. II. Mitteilung). Kraut, H., E. K. Frey and E. Bauer, Ztschr. f. phys. Chem. **175**: 97. 1928.

A substance has been isolated from normal urine (by precipitation with uranyl acetate and subsequent absorption on infusorial earth) which will cause a definite increase in pulse amplitude lasting for a minute when injected into a dog in half milligram doses. A less pure preparation has been obtained from the blood, 60-80 cc. of blood yielding 140 mgm. of a preparation equaling in activity 0.5 mgm. of the urine preparation. Blood serum has the effect of inactivating the circulatory hormone after a period of minutes or hours, this inactivating action being destroyed by heating, acidification, addition of alcohol, filtration with infusorial earth, or digestion with papain. Following digestion wth papain and dialysis, a unit of the active material may be obtained from as little as 2 cc. of blood. The hormone is differentiated from histamine by having an opposite effect on the liver volume and carotid pressure.

—Burnham S. Walker.

Condition of endocrine organs in rickets and spasmophilia. Stoltenberg, L., Norsk. mag. f. laegevidensk. **90**: 729. 1929. Abst., J. A. M. A. **93**: 1036.

In rabbits with rickets and spasmophilia, Stoltenberg did not find morphologic changes in the suprarenals or thymus of etiologic or pathogenic significance. In the thyroid and parathyroids, hyperplasia and hypertrophy were noted and interpreted as signs of increased internal secretion. While no etiologic or pathogenic responsibility in the usual sense is ascribed to these organs, the rachitic and spasmophilic picture is influenced by their reactions.

Reactions of immature monkeys (Macacus rhesus) to injections of ovarian hormone. Allen, E., J. Morphol. **46**: 479. 1928.

Series of injections of ovarian hormone have been made into normal and ovariectomized immature animals. Injections were made twice daily for twenty-two days. The total dose exceeded 1000 rat units per animal. Effects noted in the living animals were the appearance of reddening and swelling of the "sexual skin" and change of the cell content of the vaginal smear to the interval type of the mature animal. Measurements made at operation, before and after injections, indicated considerable enlargement of both the cervix and body of the uterus. The thymus glands of the injected animals weighed significantly less than those of the controls. Histologic study of the genital tract showed extreme thickening of the vaginal walls, considerable growth of the uterine epithelium and glands, hypertrophy of the muscle layers of the uterus, and advanced differentiation of the epithelium of the uterine tubes. The ovaries of the injected normal animal were smaller and contained fewer primordial and medium-sized follicles than those of the controls. The presence of large numbers of atretic follicles, especially large flattened scars from former relatively well-developed follicles also suggests a harmful effect of this amount of ovarian hormone upon follicular development. Several stages of elimination of ova from polyovular follicles were also observed. There was marked growth in the ducts and an increase in the number of alveoli of the mammary glands.—Author's Abst.

Further experiments with an ovarian hormone in the ovariectomized adult monkey, Macacus rhesus, especially in the degenerative phase of the experimental menstrual cycle. Allen, E., Am. J. Anat. **42**: 467. 1928.

In previous experiments with active extracts of pig ovaries and human placenta, standardized quantitatively by the oestrous test in spayed rats, the reaction of ovariectomized mature monkeys was studied. The animals sacrificed in this first series were killed immediately after the last of a series of injections. The present experiments were a continuation of this work and dealt especially with retrogression in the sexual organs during the five days following the cessation of injections, the animals being killed on the first, third and fifth days after the last injections when the effects of hormone stimulation were retrogressing. Measurements of uteri showed considerable decrease in diameters by the third day and a further decrease (almost to the size of the controls) by the fifth day after the last injection. The lumen of the vagina of each animal contained masses of sloughed epithelial cells. Leucocytic infiltration of the stroma of the vaginal wall had begun by the third day and spread to the basal layers of the epithelium by the fifth day, but leucocytes had not entered the masses of epithelial cells in the lumen. Marked migration of leucocytes through the cervical glands, as described in earlier experiments, was noted in all animals. The uterine mucosa of the animals killed on the first and third days after the last injection was pale, spongy and edematous. That of the monkey killed on the fifth day was in an early menstrual stage. There was menstrual discharge in the lumen of the uterus and vagina and the endometrium was hemorrhagic. Histologic section showed a typical menstrual endometrium. Cessation of growth was indicated by a low incidence of mitosis. The edematous condition had also subsided by the fifth day after the cessation of injections. The last case added to earlier experiments makes a total of eight experimental menses in ovariectomized monkeys following withdrawal of hormone stimulation after considerable periods of injections.—Author's Abst.

Sympatheticotropic cells in the ovary and their function (Sympathikotrope Zellen im Eierstock und ihre neurokrine Funktion). Berger, L., Virchow's Arch. f. path. Anat. **267**: 433. 1928.

In 218 pairs of ovaries 168 contained sympatheticotropic cells in small groups or in masses of 100. Frequently they were intrapara- or peri-neural in distribution. Generally they were round or polyhedral, somewhat smaller than ganglion cells, possessed a round nucleus with 1 or 2 nucleoli, an eosinophic cytoplasm which frequently contained brown pigment, and occasionally the cytoplasm was vacuolated. Ten per cent contained cytoplasmic, eosinophilic crystalized bodies usually cylindrical in shape. In the testicle similar cells are associated with the interstitial cells of Leydig and show corresponding distribution and changes. This may indicate an associated internal secretory function for the sympatheticotropic cells. By analogy a similar function for the sympatheticotropic cells of the ovary is possible.—Wm. Susman.

A case of macrogenitosomia and intersexuality of gynecomastic type (Contribución al estudio de la macrogenitosomía, con descripción de un caso de sindrome macrogenitosómico, e intersexualismo puberal de tipo ginecomástico). Bonilla, E., Arch. españ. de pediat. **12**: 591. 1928.

A case of this disorder in a twelve-year-old child is described, with citation of 78 pertinent articles from the literature. The theoretical possibilities of the endocrine etiology are discussed.—R. G. H.

Effect of castration on the bones of the nose (Influence de la castration sur les cornets du nez). Campy, C. and N. Kritch, Compt. rend. Soc. de biol. **100**: 413. 1929.

In guinea pigs, rabbits, sheep, and cattle, castration is followed by an atrophy or failure in growth of the bones of the nose.—J. C. D.

Chemical sympathectomy of the spermatic cord (Simpatectomía química del cordón espermático). Cassuto, A., Rev. españ. cir y urol. **8**: 351. 1926. Abst., Biol. Absts. **3**: 583.

After reviewing the literature and concluding that the interstitial tissue of the testicle is probably not the source of hormonal activity, the author de-

scribes experiments on 18 dogs. The spermatic cord was exposed by an inguinal incision and its arteries painted with a solution of phenol for 2 cm. This treatment, which is supposed to destroy the fibres of the sympathetic nerves surrounding the arteries, resulted in an increase in size of the arteries, increased blood supply to the testicle, and, as shown by histological examination up to nine months later, increase in the size of the testicle and in the activity of the seminiferous tubules, without noticeable change in the interstitial tissue. The dogs showed improved vigor and energy and increase of libido. Similar results were obtained by operation on the ovarian arteries of 3 bitches. The author then performed the same operation (unilaterally) on 6 young men who were suffering from sexual debility; the longest period of observation since is 8 months. In every case the patient reported improved physical and mental condition and complete restoration of sexual function.

The treatment of ovarian deficiency with intravenous injections of an ovarian extract (Die Behandlung der Eierstockermüdungs-Erscheinungen mittels intravenöser Eierstockertrakt Injektionen). Cohn, B., Med. Klin. **24**: 1863. 1928.

The results of the treatment of ovarian deficiency with intravenous injections of an ovarian extract are briefly reported. A series of fifty patients ranging in age from puberty to the menopause having symptoms which were thought to be due to an ovarian deficiency were followed over a period of three years. The extract used was an albumen free, water extract of whole ovary. From one to five cc. were given at one dose. As a rule twelve injections were necessary to relieve the symptoms. Those patients who did not respond to the treatment were considered neurasthenics instead of having a true deficiency of the internal secretion of the ovary. Similar results were obtained with the diathermy when using the positive electrode in the vagina. No case reports were given.—Merrill Smeltzer.

The duration of corpus luteum activity in pregnancy (Sur la durée de l'activité lutéinique pendant la gestation). Courrier, R. and R. Kehl, Compt. rend. Soc. de biol. **101**: 345. 1929.

Pregnant rabbits in which all of the young were in one horn of the uterus were chosen and the changes in the uterine wall of the free horn were followed. These changes were similar to those following infertile mating when effects of the corpus luteum disappear after twenty-four days. In the pregnant animal, the return of the uterine wall to normal was somewhat slower but all evidence of corpus luteum influence disappeared some time before the close of pregnancy.—J. C. D.

The heterogeneous testis transplant problem as applied to white rats and mice. Crisler, G., Am. J. Physiol. **90**: 623. 1929.

Palpable well-vascularized nodules showing the persistence of tubules for five to six months resulted, in 43 experiments, from mouse testes transplanted into rats. By the criteria of the French workers about 79 per cent of these grafts were viable and functional, but by the author's criteria they had simply persisted anatomically and were degenerating.—R. G. H.

Ovarian responses. Differences elicited by treatment with urine from pregnant women and by freshly implanted anterior lobe. Engle, E. T., J. A. M. A. **93**: 276. 1929.

Previous work has shown that the daily transplantation of anterior lobe into immature female mice results in a marked follicular growth followed by ovulation. Treatment of immature female mice with the urine of pregnancy results in follicular growth, with atresia of follicle and ovum, and effective prevention of ovulation by the transformation of the follicle into a corpus luteum with retained ovum. It is difficult to consider the two types of response as being due to the same factor from the anterior lobe.—Author's Summary.

Mechanism of ovulation in the rabbit. II. Ovulation produced by the injection of urine from pregnant women. Friedman, M. E., Am. J. Physiol. **90**: 617. 1929.

It was found to be impossible to produce ovulation in the rabbit by the transplantation of as many as fifteen fresh rat hypophyses, or by the intraperitoneal injection of twenty-four rat hypophyses. Intraperitoneal injection of urine from pregnant women produced luteinization of the resulting corpora hemorrhagica in the rabbit ovary. A single intravenous injection of urine from pregnant women provoked ovulation in the rabbit. The samples of urine so far obtained from non-pregnant women have been utterly without effect on the rabbit ovary, either when injected intraperitoneally or when injected intravenously.—Author's Summary.

A case of hypogenitalism (Uber einen Fall von Hypogenitalismus). Galant, J., Virchow's Arch. f. path. Anat. **267**: 648. 1928.

The main features of hypogenitalism are: cutis marmorata, akrocyanosis, and underdeveloped genitalia. In a female patient of 23 years, the author found cutis marmorata, cyanosis of hands and feet, hypotrichosis, underdevelopment of the genitalia, and eunuchoid collections of fat. The patient began menstruating at 19 years and had been pregnant. These in all suggest the presence of a constitutional anomaly. Eunuchoidism was ruled out because of a successful pregnancy while infantalism was eliminated because of the adult mentality of the patient. He concludes that this is a case of hypogenitalism due to hypopituitarism. The literature is surveyed to a limited extent and various differential diagnoses are discussed.—Wm. Susman.

Note on folliculine in the urine of cancerous patients (Recherche de la folliculine dans les urines des cancéreux). Harde, E., P. Henri and J. Batier, Compt. rend. Soc. de biol. **100**: 491. 1929.

In patients with cancer, as in pregnant women, tissue is growing rapidly. In certain cases folliculine could be demonstrated in urine from both men and women with cancer, when the production of oestrous changes in the vagina of mice was used as a test.

New experiments with transplantation of desiccated ovaries (Weitere Untersuchungen über die Überpflanzung getrockneter Eierstöke). Kallas, H., Virchow's Arch. f. path. Anat. **273**: 524. 1929.

The question of transplantation of desiccated ovaries was examined. The results were identical with those communicated by Lipschütz. There were 8 successful cases in which the ovary suffered a loss of up to 50 per cent of weight. Similar grafts were in full endocrine function about 5 months later. The differential survival at different degrees of desiccation (per cent of loss of weight) also has been studied. Together with the nine successful experiments of Lipschütz the total number of successful cases after a loss of 60 per cent by desiccation was seventeen out of thirty. There was no positive case in a group of 11 animals in which desiccation was more than 60 per cent.

—A. Lipschütz.

Corpus luteum and glandular phase of the mammary gland in the rabbit (Corps jaune et phase glandulaire mamaire chez le lapin). Kallas, H. and L. Lipschütz. Compt. rend. Soc. de biol. **100**: 981. 1929.

Hyperfeminization in the rabbit (Über Hyperfeminierung bei Kaninchen). Bull. d'histologie appliq. à la physiol. **6**: 273. 1929.

Ovaries have been engrafted into castrated male rabbits. There was in two cases a hypertrophy of the mammary gland or hyperfeminization as formerly observed by Steinach and others in the guinea pig. The mammary gland revealed a development similar to that in pseudopregnancy as observed by Ancel and Bouin in the female rabbit under the influence of the corpus luteum. Now, the ovarian graft in the male rabbit behaved like that in the male guinea pig, i. e., there were no corpora lutea and only distended follicles. From these experiments it is concluded that mammary development, characteristic of pregnancy and pseudopregnancy, can take place during the follicular phase.

—A. Lipschütz.

The Ganglion cervicalia uteri and the oestrous hormone. Kennedy, W. P., Edinburg M. J. **36**: 75. 1929. (Transactions of the Edinburgh Obstetrical Society.)

In spayed mice this ganglion shows regressive changes, which involve the chromaffin cells and nerve cells. Injections with follicular extract and certain vegetable derivatives having a similar effect restore the ganglion to its normal appearance.—J. C. D.

Organ extracts as uterine stimulants (Organertraklgemische als Wehenmittel). Kohler, R. and H. Porges, Zentralbl. f. Gyn. **51**: 3042. 1927.

Women in the first stage of labor with varying degrees of uterine inertia were studied to determine if thymus extract has a specific effect on pituitrin which makes the combination of the two safe to be used in the first stage of labor. Extracts other than that of the thymus were used with pituitrin. Cases were briefly summarized in which organic extracts of placenta, ovary and breasts combined with pituitrin were used. No difference was noted in the effects of the various combinations. From these studies it was concluded that thymus extract has no effect on the action of pituitrin. Tetanic contraction of the uterus does occur with thymophysin and two such cases are reported. Such contraction depends on the concentration of the uterine activating substance in the body.—M. Smeltzer.

The actual acidity in single sections of the male gonadal apparatus of rats and its hormonal significance (Die reelle Acidität in den einzelnen Abschnitten des männlichen Genitalapparates der Ratte und ihre hormonale Bedingtheit). von Lanz, T., Arch. f. d. ges. Physiol. **222**: 181. 1929.

Using a hollow-needle, gold-iridium electrode, the true acidity was determined with pure hydrogen and mixtures of hydrogen and carbon dioxide, with surviving organs of normal animals, with young animals with ligatured ducti efferentes, and with one-sided and completely castrated animals. Testicular fluid has a pH of 7.19-7.37, that of the epididymis 6.48 to 6.61, while that of the prostate secretion is about 7.14. The secretion of the seminal vesicles has a pH of 6.32 to 6.34. The first and third are slightly, the second and fourth strongly buffered. The pH value is independent of spermatogenesis. Total castration influences it, the values changing to that of the blood. The internal secretion of the testis is active after ligation of the ducti efferentes.—A. T. C.

The occurrence of female sexual hormone (Menformon) in the urine of men (Über das Vorkommen weiblichen Sexualhormons (Menformon) im Harn von Männern). Laqueur, E., E. Dingemanse, P. C. Hart and S. E. de Jongh, Klin. Wchnschr. **6**: 1859. 1927. Abst., Biol. Absts. **3**: 591.

As much as 50 mouse units of female sexual hormone has been isolated from a liter of urine from men. The product has been purified so that 1 unit is contained in 0.3 mgm. of dry product.

Transplantation of conserved ovaries. II. Endocrine action of ovaries preserved at room temperature (Transplantation von konserviertem Ovarium. II. Endokrine Wirkung von bei Zimmertemperatur konservierten Ovarien). Lipschütz, A., Arch. f. d. ges. Physiol. **220**: 29. 1928.

Such ovaries are active after preservation for from 1 to 8 days at a temperature of 14-20 degrees C. Transplanted to male guinea-pigs they produce hyperfeminization. Such preservation at room temperature appears to damage them to a greater extent than when preserved on ice.—A. T. C.

Transplantation of the desiccated ovary (Transplantation von getrocknetem Ovarium). Lipschütz, A., Virchow's Arch. f. path. Anat. **272**: 245. 1929.

It was shown formerly by the writer that the ovary of the guinea-pig can be successfully grafted even after having been kept outside the body on ice or at room temperature for more than two weeks. The experiment was tried of grafting ovaries of the guinea-pig which had undergone considerable loss of water. If desiccation by exposure to $CaCl_2$ is complete the ovary never took. On the contrary, a take was possible if the loss of water was an incomplete one.

Of 21 experiments 9 were successful, with ovaries which suffered a loss of weight averaging 30 to 55 per cent. These ovaries can survive and function in the host during several months as corroborated by the histological examination of the graft 5 months after transplantation. There is no question about the action of the hormones already present in the ovary before engrafting; the experiment is successful with infantile ovaries which never before produced oestrus. Though positive results can be obtained with desiccated ovaries the experiment reveals the fact that loss of water is very detrimental to the organ. The number of successful cases when fresh, normal ovaries were used was about 85 per cent. When partly desiccated ovaries were used the number of successful cases was much less. There were also a considerable number of cases in which the graft had taken and functioned but became absorbed later on. The time of latency with partly desiccated ovaries is also lengthened. The microscopical examination of the desiccated ovary before transplantation reveals the fact that the primary follicles suffer retraction under the influence of the loss of water.—Author's Abst.

Relations between the quantity and the action of female sexual hormone (Beziehungen zwischen Menge und Wirkung des weiblichen Sexualhormons). Lipschütz, A., Biochem. Ztschr. **215**: 222. 1929.

The principles of the biological assay of the follicular hormone are discussed, comparing less purified extracts from the urine with highly purified ones. Less purified extracts produce when 100 or 200 units have been injected, a cornified stage of 1 to 2 weeks' duration; the same number of units of a highly purified extract (about 1 to 3/1000 mgm.) produces a cornified stage of only about 2 days. The number of injections is very important with highly purified extracts; if one takes as a unit the quantity which when distributed in 6 injections during 60 hours produces the cornified stage in the majority of the animals of the group, then a hundred units given in one injection will produce a lower percentage number of cases with oestrus than one unit. The reaction of the mouse to the follicular hormone is not influenced by diuresis; 1 cc. of water, of Ringer solution or of Ringer of double concentration can be given daily for several days without influencing the duration of the cornified stage after injection of great quantities of hormone. The all-or-nothing law as applied to the follicular hormone is also discussed. It is shown that the law is in accordance with all experimental data available. Oestrus is evidently produced when a certain concentration of hormone persists for a certain time. The incomplete reaction can be explained, assuming that in these cases the threshold concentration did not persist long enough. The necessity of establishing international rules for the biological assay of the follicular hormone is insisted upon.—Author's Abst.

Oxygen use of the isolated ovary of the mammal (Über den Sauerstoffverbrauch des isolierten Säugetierovariums). Lipschütz, A., Arch. f. d. ges. Physiol. **223**: 56. 1929.

New observations on the metabolism of the isolated ovary (Nouvelles observations sur le métabolisme de l'ovaire isolé). Compt. rend Soc. de biol. **100**: 982. 1929.

The oxygen consumption of the isolated ovary of the guinea-pig was studied under different experimental conditions. There is an oxygen use for several days at temperatures lower than 38 degrees C., even on ice. The difference between oxygen use at various temperatures is $Q_{10}=2$, 5, in such a manner that oxygen use on ice was about 20 to 40 times less than at body temperature. Oxygen use per mgm. of ovary of the guinea-pig is about one-third as much as in the mouse. The law of "liminal thickness" of Warburg has to be taken into consideration when the maximal oxygen use of the ovary is examined. The better results with transplantation of isolated ovaries when kept on ice can be explained on the assumption that oxygen use being highly reduced at low temperatures the thickness of the ovary is not greater than the liminal thickness at this low temperature. If the isolated ovary has been kept at temperatures lower than 0°, there is an oxygen use when examined afterwards at about 18°, but it diminishes rapidly during 24 hours; at body temperature such an ovary shows oxygen use only for a short time. The same phenomenon is seen in triturated ovaries. Freezing of the ovary is thus identical with mechanical destruction of the organ.—A. Lipschütz.

Castration in the pigeon (Castration chez le Pigeon). Lipschütz, A. and O. Wilhelm, J. de physiol. et de path. gén. **27:** 1. 1929.

The plumage of the male pigeon is not influenced by castration when observed during more than 14 months. Sexual behavior seems to be influenced. A testicular fragment, if not too small, is able to protect against loss of sexual behavior. Absence of sexual demorphism in the plumage of birds can be evidently caused in two different ways: (1) the feather germ is influenced by ovarian and testicular hormones (Sebright type; Morgan Roxas); (2) the feather germ is influenced neither by ovarian nor by testicular hormones (Columba type).—A. Lipschütz.

Note on the properties of urine from pregnant women (Contribution a l'étude des propriétés de l'urine de femme gravide). Orban, F. and M. Watrin, Compt. rend. Soc. de biol. **100:** 435. 1929.

Interpretation of the changes induced in the ovaries of young mice by urine from pregnant women (Sur l'interpretation des phénomènes provoqués dans l'ovaire impubère de souris par l'injection d'urine de femme gravide). Orban, F. and M. Watrin, Compt. rend. Soc. de biol. **100:** 438. 1900.

Urine from pregnant women has a specific effect peculiar to itself on the ovaries of mice before puberty. This effect is not that of the "prehypophysine," but is characterized by intense congestion of the ovary with rupture of the capillaries; an exaggeration of normal degenerative changes. The vaginal changes in mice under these conditions are not a safe guide to the ovarian. —J. C. D.

Can senescence be retarded (La vechiaia puo essere ritardata)? Pende, N., Scientia, **42:** 11. 1927. Abst., Biol. Absts. **3:** 593.

The endocrine mechanism operates throughout the life of the individual in a series of normal changes, which may be modified by heredity, function, and interaction of different endocrine glands. If the whole process is clearly apprehended, it may lead to such use of endocrine therapy as to ward off premature senility.

"Progynon"-Schering—A new cyclus hormone preparation ("Progynon"-Schering, ein neues Zyklus-Hormonpräparat; Amenorrhöe [ohne und mit Hypoplasia Genitalis]). Streck, A., Klin Wchnschr. **7:** 1172. 1928.

Progynon is an aqueous solution of the placenta of the cow, prepared commercially in the form of suppositories or pills. It has the property of stimulating estrus. It has been standardized by the Allen, Doisy rat unit biological test and tested clinically by use of the Aschheim Zondek technique of recovering the hormone in the urine. The authors used animals and women to test the toxic effects and found no local, general, protein or toxic results even after enormous doses, given orally or rectally. The study revealed that an initial dose of 250 rat units or 500 rat units was required, repeated every day or every other day and that the summation of dosage necessary to produce menstruation was 500 to 4,500 units given in from two to eighteen doses, and that treatment took from one to five weeks. The results were better and more lasting the oftener the menses had occurred before treatment and the less marked the genital hypoplasia. The author also considers the causes of hypoplasia genitalis, and gives the result of a study of twenty-six cases of amenorrhea with or without hypoplasia genitalis. Six typical case histories are cited. The use of progynon is indicated in cases with ovarian hypofunction and genital hypoplasia, and contraindicated in cases with hypogenitalism where there is a general disease or inflammation of the genital organs. In conclusion the author emphasizes the value of oral and ambulatory treatment, the use of large initial doses and a summation of 500 to 4,500 rat units required, and that the results are those of substitution. The best clinical criterion of the value of the product is the recurrence of menstruation.—F. Firestone.

Eczema and ovarian disturbances (Ekzem und Ovarialstörungen). Szego, P., Zentralbl. f. Gynäk. **52:** 1593. 1928.

This is a report of the results of glandular therapy in 16 cases of dermatitis and eczemas associated with disturbances of ovarian function. Little

therapeutic effect was noted on skin diseases associated with hypermenorrhea, whereas good results were obtained when the skin disease was associated with oligomenorrhea or amenorrhea, even in pregnancy and the climacteric. Other systemic conditions were not excluded. In the treatment of the reported cases "glanduovin" was used intravenously and intramuscularly on alternate days. The dosage varied from 2 to 5 cc., a total of about 60 cc. being given in a course of 16 injections. With this treatment the itching of the external genitalia disappeared and normal menstruation was re-established.—M. R. White.

Experiments with extraction of the female sexual hormone from the urine of the pregnant woman (Über Versuche zur Gewinnung des weiblichen Sexualhormons aus dem Harn der Schwangeren). Veshnjakov, S. and A. Lipschütz, Biochem. Ztschr. **210**: 348. 1929.

A description is given of a simple method of extraction of follicular hormone from the urine of pregnant women following the manner of Zondek and Aschheim. One liter of alcohol is added to 10 liters of urine; the alcohol is evaporated and the residue is extracted with ether; the extraction is repeated several times. After evaporation of the ether the residue is treated with 10 per cent NaOH. Extraction with ether is again repeated several times. Repeated extraction with ether and water gives a pruity of about 1/1000 mgm. per M. U.—A. Lipschütz.

The hormone of heart movement. XI. Further experiments with the heart-hormone preparation (Ueber ein Hormon der Herzbewegung. XI. Weitere Froschherzversuche mit dem Herzhormon präparat). Haberlandt, L., Arch. f. d. ges. Physiol. **221**: 576. 1929.

Extracts completely free from histamine give the effects previously described by the author.—A. T. C.

Further experiments on the heart hormone. The active principle of Haberlandt's frog-heart hormone (Fortgesetzte Untersuchungen über das Herzhormon. Der wirksame Bestandteil des Haberlandtschen Froschherzhormons). Rigler, R., Arch. f. d. ges. Physiol. **221**: 509. 1929.

The action attributed by Haberlandt to an internal secretion is due to the combined effect of potassium ions and certain alcohol-ether soluble compounds (described by A. J. Clark and by Loewi) with a positive inotropic effect.
—A. T. C.

Hypophyseal cachexia (Uber einen Fall von hypophysarea Kachexie). Altmann, F., Frankfurt Ztschr. f. Path. **36**: 393. 1928.

In a woman of 48 cachexia, loss of hair, dry skin, fine tremors, atrophy of genitalia, lead to a diagnosis of hypophyseal cachexia. At death the complete clinical diagnosis was caseous pneumonia, epilepsy, severe anaemia, and pluriglandular endocrine insufficiency. At autopsy there was found a large pineal body, extreme atrophy of the hypophysis, caseous pneumonia of the left lung, extreme atrophy of the thyroid, large kidneys and small adrenals rich in lipoids. Microscopic examination showed the pars glandularis of the hypophysis represented by only a few cells and no evidence of inflammation. The thyroid parenchyma was degenerate as well as atrophic. The adrenal medulla was much reduced in size. In the kidneys there were fatty degeneration of the tubules and arteriosclerosis. In all the essential feature is a disease of the endocrines with the primary lesion in the pituitary. That the tubercular process is the primary cause of endocrine lesions can not be substantiated. The more likely cause is some constitutional and endogenous factor as in pre-senile involution—Wm. Susman.

Laurence-Biedl disease (Ein Beitrag zur Laurence-Biedlschen Krankheit). Bernhardt, H., Ztschr. f. klin. Med. **107**: 488. 1928.

Laurence-Biedl disease includes Frohlich's syndrome together with retinitis pigmentosa, optic atrophy and polydactylia and psychical disturbances. In all there are 20 recorded cases. Two further cases are here described, with complete histories. Two brothers 16½ and 10¾ years of age showed dystrophia adiposo-genitalis, polydactylia, mental underdevelopment and enlarge-

ment of the sella turcica. The younger had diabetes insipidus also. Numerous metabolic and biochemical tests were made and the results discussed. In treatment, thyroidin and calcium were beneficial. The author concludes that the optic atrophy, polydactylia and the mental underdevelopment point to a congenital origin but that the dystrophia adiposo genitalis is due probably to a disturbance of the hypophysis and mid brain.—Wm. Susman.

Report of several cases of diabetes insipidus treated with powdered posterior lobe by nasal administration (Quelques cas de diabete insipide traites par la poudre hypophysaire [lobe posterieur] administres par voie nasal). Choay, A. and L. Choay, Rev. franç. d'endocrinol. **6**: 423. 1928.

Nasal applications of powdered gland give results similar to hypodermic injections, but more gland, by weight, is required to produce equivalent results. There seems to be no more danger in this method than in the hypodermic, and it is considered more convenient.—B. C.

Precocity from hypopituitarism. Elias, L. W., South. M. J. **22**: 595. 1929.

The author reports two cases of sexual precocity in girls, which he thinks is due to hypopituitarism. The first case is that of a 3-year-old girl who weighed 6½ pounds at birth, 45 at 9 months and now weighs 114 pounds. She has a vaginal discharge which has continued at intervals of from six to eight weeks for the past year. It is yellowish or slightly pink at times. The second case is a colored girl of 9 years who has the appearance of one of 13 years. She is mentally backward. There is a heavy growth of pubic and axillary hair which has been present for the past two years. The breasts are well developed. The clitoris is not enlarged. There is no history of precocious menstruation in her family. Menstruation began at the age of two years and has been regular every four weeks ever since, lasting about three days at a time. The character of the flow is normal.—M. B. G.

Anterior pituitary hormone in blood during pregnancy. Fluhmann, C. F., J. A. M. A. **92**: 1744. 1929. Abst., A. M. A.

A study was made to obtain some information regarding the presence of hormones, and particularly the anterior pituitary hormone in the blood of pregnant women, and to note the changes set up in the genital organs of immature female white mice following the injection of human blood serum. The reactions found in the genital organs of immature white mice following the injection of blood serum from pregnant and nonpregnant patients may be classified in three groups, those attributed to the effects of a hormone from the anterior pituitary gland being considered the most important. One hundred patients were examined. Forty-eight represented normal pregnancies, and of these two gave negative results, 11 showed the presence of ovarian hormone alone, and 35 were positive for anterior pituitary substance. Of 52 controls, two patients showed ovarian hormone, and six anterior pituitary hormone. Of the latter, four were patients with either an operative or a radiation castration, and two had a functional amenorrhea.

Mechanism of the influence of pituitary extracts on blood sugar (Beiträge zum Mechanismus der Blutzuckerbeeinflussung durch Hypophysenextrakte). Fritz, G., Arch. f. d. ges. Physiol. **220**: 101. 1928.

Intramuscular injection of posterior pituitary extract into mammals increases the blood sugar. The action is secondary to adrenine mobilization, for it is not produced in adrenalectomized animals. The adrenine mobilization is a result of general stimulation of the sympathetics.—A. T. C.

Case of pituitary tumor treated by X-rays. Griffith, A. D., Proc. Roy. Soc. Med. Sect. Ophthal. **22**: 31. 1929.

In a case of pituitary tumor occurring in a male of 48, the headache, giddiness, and staggering were accompanied by difficulty in reading. Examination revealed central bi-temporal scotomata. Twenty-six X-ray treatments of the pituitary resulted in a disappearance of headache and giddiness, a gradual improvement of the fields of vision and finally the ability to read normally.—I. B.

Function of the hypophysis and region of the tuber cinerium and infundibulum in the toad (Les functions de l'hypophyse et de la région infundibulo-tubérienne chez le Crapaud). Houssay, B. A. and L. Giusti.

The hypophysis and the testis in the toad Bufo Marinus (L.) Schneid (L'hypophyse et le testicule chez le Crapaud Bufo marinus [L.] Schneid). Houssay, B. A. and J. M. Lascano-Gonzales, Compt. rend. Soc. de Biol. **101**: 935, 938. 1929.

Numerous and carefully controlled experiments involving extirpation of the hypophysis and deliberate injuries to the infundibular region brought out first a hyperactivity of the gland, marked by a darkening of the skin at the moment of operation and then pallor, testicular atrophy, asthenia, and convulsions with a corresponding rise in mortality. Pallor is a specific symptom dependent on loss of the pars intermedia. The other symptoms are seen less frequently where the anterior lobe alone is removed. The formation of a cutaneous pellicle, discharge of immature ova, and polyuria are seen in total hypophyseal removal but especially in cases of infundibular damage. The symptoms of hypophyseal extirpation can be prevented by frequent transplants of toad pituitary.—J. C. D.

The anti-diuretic action of separated principles of the posterior lobe of the pituitary body. Hemingway, A. and J. M. Peterson, J. Physiol. **67**: 24. 1929.

Perfusion of heart-lung-kidney preparations with blood to which was added vasopressin and oxytocin, shows that both have prolonged anti-diuretic effects, that of vasopressin being the more powerful. This substance also increases the resistance of the kidney capillaries and diminishes the renal blood flow. There is an accompanying increased chloride concentration and an increased total output of chloride.—C. J. R.

Acromegaly with reference to eye and ear findings. Hertz, W. J., Atlantic M. J. **32**: 768. 1929.

This is a report of a case of acromegaly of more than 8 years' duration occurring in a white woman of 28. In July, 1928, the patient complained of earache. Examination showed a bulging tympanic membrane which was incised, with relief of symptoms. A few weeks later ear discomfort returned. Because of a previous history of diabetes a diabetic regime was outlined. The patient was admitted to the hospital where it was discovered that the blood sugar was 440 mgm. per 100 cc. and the Wassermann reaction was 4 plus. Urinalysis revealed a trace of albumin and 2.2% sugar, although it was negative for acetone, diacetic acid and casts. Insulin and anti-luetic medication was now given. On September 6th the right mastoid antrum was opened and a large abscess evacuated. On the fourth day after operation the temperature rose to 101.2 and patient complained of dizziness. At this time spontaneous nystagmus toward the affected side was observed. This, however, disappeared and the temperature became normal in 48 hours after removal of the iodoform gauze packing in the wound. The patient then developed an acute mania with a septic type of temperature and died on the ninth day after operation. A postmortem was not permitted.—I. B.

Antagonism between the hypophysis and insulin in the toad (Antagonisme entre l'hypophyse et l'insuline chez le Crapaud). Houssay, B. A. and Dora Potick, Compt. rend. Soc. de biol. **101**: 940. 1929.

The authors demonstrated that posterior lobe extract injected twenty-four hours after an injection of insulin reduced the inhibitory power of the former without interfering with its oliguric action. The melanophores were over expanded. Removal of the hypophysis makes the toad very susceptible to the toxic effects of insulin. Removal of the glandular lobe has somewhat less effect and cauterization of the infundibular region has no influence. Extracts of bovine anterior and posterior lobes protect against this toxic action in hypophysectomized toads. Daily grafts of toad anterior lobe protects against insulin toxemia while posterior lobe implants are ineffective.—J. C. D.

Treatment of constitutional obesity with hypophyseal preparations. Hunt, T. C., Wien. klin. Wchnschr. **41**: 1682. 1928.

Hunt reviews the literature bearing on the effect of posterior lobe extract on fat metabolism. It has been accepted that pituitrin causes mobilization of fat, increasing the store in the liver where it is evidently metabolized. According to Raab, during the state of fasting in dogs, it reduces the amount of fat in the blood. Hunt undertook some experimental studies in four patients suffering with constitutional obesity, in which he used various extracts of the posterior lobe administered subcutaneously. The injections were given daily and varied in number from 6 to 13. He failed to get any reduction in weight. This is contrary to the results obtained by Langdon Brown, who reported a case in which there occurred a marked reduction in weight following injections of pituitrin. Hunt concludes that his experiments do not justify the use of posterior lobe preparations to produce loss in weight.—H. G. Beck.

The action of extract of pituitary on the blood sugar after pancreatectomy. Imrie, C. G. J., J. Physiol. **67**: 264. 1929.

In dogs, after pancreatectomy, if insulin is withheld 44 hours or less, a rise in blood sugar results from pituitary extract as in intact animals. After 70 hours without insulin, this rise does not occur. Under the latter conditions adrenalin also fails to increase blood sugar. Muscle glycogen is not affected, therefore the hyperglucemia is due to hydrolysis of liver glycogen.
—C. J. R.

Precocious sexual maturity induced by parabiosis (Puberté précoce par parabiose). Kallas, H., Compt. rend. Soc. de biol. **100**: 979. 1929. **Parabiosis and anterior lobe of the hypophysis (Parabiose und Hypophysenvorderlappen).** Arch. f. d. ges. physiol. **223**: 232. 1929.

When two infantile rats weighing about 15 grams each, one castrated, the other not castrated, are parabiotically united, a precocious sexual maturity is established in about 7 days in the uncastrated animal. The vaginal mucosa is keratinized, the uterus undergoes the characteristic changes of oestrus. Oestrus can persist 6 days without interruption. There is follicular ripening in the infantile ovary under the influence of the castrated parabiotic partner. At the end of the second week corpora lutea are produced and oestrus is interrupted. Since these phenomena are identical with those observed after hypophyseal injections into an infantile animal, it is concluded that the changes as observed in the genital region in parabiosis are to be explained by hypophyseal substances passing from the castrated animal to the uncastrated one. This is corroborated by the experimental fact that production of sexual maturity in the uncastrated partner can be hastened by hypophyseal injections into the castrated one. Passing of hypophyseal substances from the castrated partner into the uncastrated one begins a few days after establishing the parabiosis. Since sexual maturity is produced by parabiotic union with an infantile castrate it is concluded that the hypophysis of the infantile animal is able to produce and to secrete the X-substances in question. The fact that sexual maturity in the uncastrated partner is produced only if the ovaries of the castrated partner have been removed, indicates that the infantile ovary acts in some way on the hypophysis.—A. Lipschütz.

Law of follicular constancy, law of puberty and anterior lobe of the hypophysis (Ley de la constancia numerica folicular, ley de la pubertad y lobulo anterior de la hypofisis). Lipschütz, A., Bol. de la Soc. de Biol. de Conc. **2**: 3. 1929.

The qualities of the hypothetical X-substances postulated from the facts expressed in the law of follicular constancy and the law of puberty, and the properties of the hypophyseal substances are identical; both are similar in male and female, both are produced in the normal and in the castrated animal, both are used in the glands as supposed by Sand. Since there is a complete parallelism between both sets of experimental data, the author believes that the hypophysis is responsible for the production of the X-substances.
—Author's Abst.

Hypophysis and law of puberty (Hypophyse und Gesetz der Pubertät). Lipschütz, A., H. Kallas and R. Paez, Arch. f. d. ges. Physiol. **221**: 6. 1929.

The hypophyses of male and female guinea-pigs were able to produce sexual precocity in infantile female mice even when the donor had been castrated for more than a year. The hypophysis was active when taken from a male guinea-pig hyperfeminized by ovarian transplantation. There was a precocious follicular development but no formation of corpora lutea. A single hypophysis of a new-born guinea-pig usually produced sexual precocity in the infantile mouse. The experiments of Smith and Engle with the infantile hypophysis of the rat are corroborated by the above experiments. The hypophysis of an old dog (14 years) was also active in producing precocious development in the infantile female mouse.—A. Lipschütz.

The pituitary and the law of puberty (Hypophyse und Gesetz der Pubertät). Lipschütz, A., H. Kallas and R. Paez, Arch. f. d. ges. Physiol. **221**: 695. 1929.

The anterior pituitary of castrated male and female guinea-pigs acts in the same way on the uterus of the infantile mouse as does the normal pituitary, even when castration had been performed more than a year previously. The pituitary of hyperfeminized guinea-pigs is simalrly active, as is also that of the young rat, and the young guinea-pig of either sex. Similar effect on the uterus was obtained by injection of the pituitary of a senile dog. Smith and Engle's conclusion that the anterior pituitary of the infantile animal already produces its secretion and that of the aged animal still produces it is confirmed.
—A. T. C.

Epilepsy in children. McQuarrie, I., Am. J. Dis. Child. **38**: 451. 1929.

There seems to be a tendency for epileptic subjects to retain water during the active stage of the disease in amounts which are harmful. Convulsions tend to increase when there is a positive water balance while diuresis favors the prevention of further seizures. Parenteral administration of the solution of pituitary or of the antidiuretic hormone of the hypophysis causes the development of a positive water balance and the occurrence of seizures.—M. B. G.

The antidiuretic effect of solution of pituitary dropped intranasally in a case of diabetes insipidus. Mettel, H. B., Am. J. Dis. Child. **38**: 342. 1929.

A case of diabetes insipidus in a girl 9 years of age is reported, with all the physical and laboratory findings. Charts are given showing the effect on the urinary output of the administration of pituitary extract subcutaneously and intranasally. Equal effects were obtained by each method. There was a marked increase in weight of the patient. It is concluded that the intranasal application of posterior pituitary solutions is as efficacious as other methods heretofore described. Attention is drawn to the unusual gain in weight, and comments are made concerning the relation of this result to the function of the pituitary gland.—Author's Abst.

Specific dynamic action and the pituitary. (Rat experiments.) (Ueber spezifisch-dynamische Wirkung und Hypophyse [Rattenversuche]). Nothhaas, R., Arch. f. d. ges. Physiol. **221**: 763. 1929.

Feeding anterior pituitary substance to rats caused a slight increase in the specific dynamic action.—A. T. C.

The effect of anterior lobe hormone on gaseous metabolism in rabbits (Uber den Einfluss des Vorderlappenhormons auf den Gaswechsel beim Kaninchen). Reiss, M. and K. A. Winter, Endokrinol. **3**: 174. 1929.

The authors injected into rabbits and dogs extract of anterior lobe pituitary or preparation of the sex-stimulating pituitary product obtained from urine by Biedl's method. They obtained marked stimulation of the vagina and breasts and, in 2 dogs, milk production. The maturation of true corpora lutea was hastened. The blood cholesterin was increased in normal but not in ovariectomized animals. Clean-cut evidence of an influence of pituitrin on blood cholesterin was not obtained.—R. G. H.

Congenital and familial disease characterized by an adiposogenital dystrophy (Maladie congénitale et familiale caractérisée par une dystrophie adiposo-génitale associée à une rétinite pigmentaire et une polydactylie). Ricaldoni, A. and A. Isola, Arch. de méd. d. enf. **32:** 27. 1929.

The authors reported four cases, brothers and sisters who were the only survivors of a family of eight children. The four children were afflicted with the same malady, and exhibited obesity of the hypophyseal type with sexual hypoplasia, retinitis pigmentosa, polydactylism, and psychic abnormalities. Visual disturbances consisted of diminution of vision, which appeared in all the children at an early age, hemianopsia, and contraction of the visual field. Nystagmus was also mentioned. Polydactylism occurred in all of the children in the form of supernumerary fingers or toes. These were always inserted on the outer side of the metacarpal or metatarsal joints. All four children were timid, very emotional and mentally deficient. Laboratory examinations were essentially negative except roentgenograms of the skull, which showed small sella turcica with elongation of the clinoid processes. There was no delay of epiphyseal union. Both parents were normally developed and healthy. Reference is made to the report of similar cases by Bardet, Farnes, Biedl, and others. No satisfactory explanation is offered as the cause of the disease. The authors stress the familial character of the malady.—H. G. Beck.

Classification of the hypophysis syndromes (Essai de classification des syndromes hypophyso-tuberiens). Richard, G., Rev. franç. d'endocrinol. **7:** 224. 1929.

After examining the several methods of classifying the syndromes of pituitary origin, a new classification is proposed, namely, (1) systemic symptoms including (a) abnormal osteology and (b) nutritive disturbances, (2) non-systemic such as migraine and epilepsy, (3) pluriglandular symptoms.—B. C.

Hormonal activity of anterior lobe of hypophysis of fetus (Untersuchungen über die hormonale Wirksamkeit des Hypophysenvorderlappens des Fötus im Tierversuch). Schultze-Rhonhof, F. and R. Niedenthal, Zentralbl. f. Gynäk. **53:** 902. 1929.

Anterior lobes of the hypophyses of fetuses were tested for the hormone which influences the ovary. The test animals were 6 to 8 gram mice. Subcutaneous implants were made after the method described by Smith and Engle and by Zondek and Aschheim. Three human fetuses of 30, 35 and 41 cm. and several fetuses of cattle were used as sources of anterior lobes. Stimulation of growth of follicles occurred in many cases with oestrous growth in the vagina and uterus. Although in some cases ovarian stimulation did not induce ovulation, enough growth resulted to justify the conclusion that the anterior lobe of the hypophysis of the fetus has already begun secretion of the hormone which influences the ovaries.—E. A.

Water intoxication in cases of diabetes insipidus. Snell, A. M., M. Clin. North America, **12:** 1667. 1929.

A valuable paper on postencephalitic diabetes insipidus with three case histories. This form of diabetes insipidus differs from that due to other lesions in the variability of intake and output and in response to pituitrin. In certain cases a compulsion thirst may exist which may amount also to a mania for water; this thirst when existing in patients with defective judgment may lead to the consumption of enormous quantities of fluid. If their fluid intake is unrestricted or if the output of urine is reduced by pituitrin, there may be episodes undistinguishable from experimental water intoxication in animals. —I. B.

Experimental diabetes insipidus. Towne, E. B., Arch. Surg. **18:** 1165. 1929. Abst., Arch. Neurol. & Psychiat. **22:** 1055.

Towne attempted to produce diabetes insipidus in dogs by detaching the stalk of the pituitary gland. He found that the polyuria thus produced was transitory. He has searched through the literature and found that separation of the stalk rarely if ever produced permanent polyuria. From his experiments and from the literature he feels that the neurogenic theory of Camus and Roussy is not supported. He believes that these experiments strongly suggest

that diabetes insipidus is due to suppression of the secretion of the pars intermedia and the pars tuberalis.

Insulin in acromegalic diseases. Ulrich, H., Arch. Int. Med. **43**: 785. 1929.

This article refutes the widely held opinion that insulin is as effective in hyperpituitary diabetes as it is in so-called pancreatic diabetes. The evidence upon which this opinion is based is analyzed, and most of it is shown to be fallacious. As a consequence, it is suggested that insulin be used for diagnostic purposes in cases of glycosuria that are suspected of having a hypophysial foundation. A demonstrable failure of insulin to produce its expected and usual results should be regarded as a link in the chain of evidence leading to a diagnosis of hyperpituitary disease.—Author's Abst.

Action of posterior lobe extract on the tension of the cerebrospinal fluid (Action d'un extrait rétro-hypophysaire sur la tension rachidienne). Urechia, C. I. and L. Dragomir, Compt. rend. Soc. de biol. **100**: 384. 1929.

Subcutaneous injection of posterior lobe extract increases the pressure of the cerebrospinal fluid in about half an hour.—J. C. D.

The action of insulin on the liver (Über die Einwirkung des Insulins auf die Leber). Forsgren, E., Acta med. Scandinav. **70**: 139. 1929.

It was found, in a control series of eight rabbits, that the glycogen content of the liver after about 5½ hours' fasting varied from 1.8 to 9.3 per cent. The histological findings presented corresponding variations, the lobules in what the author calls "the assimilatory stage of the functional cycle of the liver" containing much glycogen, and in "the secretory stage" very little. Nine rabbits were examined after about 5½ hours' fasting, in the course of which they had been given different amounts of insulin. The glycogen content showed variations similar to those in the control series, and the values showed no relation to the insulin dosage. The author suggests that insulin convulsions do not bring about a low glycogen content of the liver, but rather that the animals in "the secretory stage" are more susceptible to insulin intoxication. Insulin does not disturb the normal cycle of the liver function, nor does it promote the deposition of glycogen.—S. Wiking.

A study of the blood pressure of patients with diabetes mellitus. Adams, S. F., Am. J. M. Sc. **177**: 195. 1929.

The blood pressures of 1001 diabetic patients in the Mayo Clinic were determined. The author chose an arbitrary standard of 150 mm. for systolic and 100 mm. for diastolic as indicating hypertension. The percentages in this series of cases were compared with blood pressure records of people who applied for insurance which were taken as normal for purposes of comparison. There was a greater percentage of hypertension among the diabetics than in the normals. The same, however, was true for hypotension. The author feels if hypertension is present, it is due to an associated abnormality and not to diabetes.—E. L.

Hyperinsulinism. Allan, F. N., Arch. Int. Med. **44**: 65. 1929.

Hyperinsulinism due to overproduction of insulin from a tumor of the islands of the pancreas is now established as a disease entity. It is probable that hyperinsulinism may also be due to a functional disturbance of the pancreas. The differential diagnosis of hypoglycemia due to hyperinsulinism and hypoglycemia due to selective hepatic insufficiency is a difficult clinical problem. Two criteria may have value in differentiation; the effect of epinephrine hydrochloride and solution of pituitary, and the amount of sugar required to maintain the blood sugar level. When the hypoglycemic tendency is so strong that the patient is incapacitated, surgical treatment appears to promise relief. Three cases are described in which there was a constant tendency to severe hypoglycemia attributed to hyperinsulinism. In case 1, there was a carcinoma of the islands of Langerhans. In case 2, surgical exploration revealed a normal appearing pancreas. Resection of a part of the pancreas was followed by considerable relief. In case 3, in which medical treatment alone was given, the patient is still under observation.—Author's Summary.

Transplantation into a series of rats of two fragments of Jensen's sarcoma, one piece normal and one treated with insulin in vivo. Difference in development of these (Transplantation, a une série de Rats, de deux fragments de sarcome de Jensen, l'un normal, l'autre insulinisé in vivo. Différence de développement de ces tumeurs). Barral, P. and R. Cade, Compt. rend. Soc. de biol. **101**: 1141. 1929.

White rats, carrying the sarcoma, were given 40 to 55 units of insulin in eight hours. These furnished the insulin treated grafts, while tumor-bearing rats without treatment furnished the control tumor grafts. Two grafts, one insulin treated and one control, were implanted into each experimental rat in symmetrical positions in the body. The grafts from the tumors in the insulin-treated rats invariably outgrew those from the controls.—J. C. D.

Histological research on islands of Langerhans in experimental scurvy (Ricerche istologivhe sulle isole di Langerhans nello scorbuto sperimentale). Borghi, B., Arch. Ist. Biochim. Ital. **1**: 69. 1929.

Guinea pigs on a scorbutic diet show the islands of Langerhans increased in size and mostly formed of chromophile cells. Guinea pigs on a "scorbutogenic" diet and injected with glucose showed a different result according to the epoch of the sugar treatment. With glucose injected at the beginning the islands looked smaller than the average, when the glucose was injected after a certain period of the "scorbutogenic" diet some hypertrophic islands were seen. The most of the island cells were chromophobe. The hyperplasia and hypertrophy of the insular tissue in the guinea pigs on a "scorbutogenic" diet are held as an effort to compensate the increased glycemia.—G. V.

Modifications in the secretion and motility of the stomach by the action of insulin and synthalin (Modificaciones de la secrecion y motilidad gastrica por accion de la insulin y sintalina). Bustamante, Garcia, Arch. d'Endocrinol. y Nutricion, **1**: 295. 1928.

Insulin increases the secretion, motility and emptying time of the stomach though not in a constant manner. This leads some authors to believe that insulin acts on the parasympathetic nervous system. Synthalin, however, diminishes the gastric secretion but augments motility and emptying time. It is suggested that this property of insulin might be utilized in cases in which stimulation of acid secretion and gastric contractions are desired, as for example in asthenia with hypochlorhydria. In case of diabetics in whom, for special reasons, gastric accumulation is not desired, the concomitant use of atropin is suggested.—E. B.

The functional test of the pancreas (Ueber die Funktionsprüfung des Inselorganes). Depisch, F. and R. Hasenöhrl, Klin. Wchnschr. **7**: 1631. 1928.

The capillary blood-sugar curve shows the influence of insulin and its antagonists on the liver, but it is not able to give any certain data as to the absolute degree of action of the internal secretion of the pancreas. In following simultaneously the capillary and venous blood-sugar curve after a sugar test meal, it is possible to measure indirectly the intensity of insulin production by the difference between the glycemias. In normal individuals there exists usually a pronounced difference between them, while in diabetes very often no difference can be found. In cases of a progredient adiposity one finds an abnormally great difference between the sugar curves, the same case showing asthenia under insulin treatment. After a prolonged fast the difference between the capillary and venous blood diminishes.—Josef Charvat.

Pancreatic-ovarian antagonism (Antagonisme pancréatico-ovarien). Fonseca, F. and C. Trincao, Compt. rend. Soc. de biol. **100**: 425. 1929.

In man, injections of ovarian extract raise the blood sugar.—J. C. D.

Glycosuria and diabetes. Galambos, A., Ann. Int. Med. **2**: 1328. 1929.

The author states that not only the inability of the diabetic to oxidize carbohydrate with attendant incomplete oxidation of the fats should be considered but also that the independent metabolic disturbance of protein metabolism should be considered. In severe diabetes mellitus as well as after experimental

removal of the pancreas in dogs, hyperaminosuria is present. The author also believes that in phloridzin diabetes the animal loses the ability to burn dextrose because the R. Q. is low.—E. L.

Cholesterol in blood of diabetics treated at the New England Deaconess' Hospital. Hunt, Hazel M., New England J. Med. **201**: 659. 1929.

The report is based on cholesterol values in 270 diabetic patients and 40 normals. The data are tabulated, analyzed, and summarized. Insulin treatment maintains the cholesterol value within normal limits. These values are lower than in pre-insulin days. Cholesterol values seem a safer guide to the patient's condition than blood-sugar readings.—J. C. D.

Diabetes mellitus: A further study of the etiology of the disease. Krantz, J. C., Ann. Int. Med. **2**: 1209. 1929.

Several other investigators have reported that the blood of a diabetic contains a virus which will produce hyperglycemia and glycosuria. Rabbits were injected intravenously and also subcutaneously with diabetic urine. Though this urine was toxic there was no hyperglycemia or glycosuria. When serum broth which was inoculated with diabetic urine was injected subcutaneously no hyperglycemia or glycosuria was produced. Using the toxicity of urine inoculated broth on the seedlings of Lupinus Albus according to the method of Macht, it was shown that the diabetic urine was no more toxic than normal urine.—E. L.

Studies in crystalline insulin. VIII. The isolation of crystalline insulin from fish islets (cod and pollock) and from the pig's pancreas. The activity of crystalline insulin and further remarks on its preparation. Jensen, H., O. Wintersteiner, E. M. K. Geiling, J. Pharmacol. & Exper. Therap. **36**: 115. 1929.

A comparative study of insulin from different sources was made. Methods of preparation are described in detail. Analyses showed close agreement in chemical constitution with beef insulin. Crystals were of the same shape but smaller. Physiological activity was found to be 25 international units per mgm. as compared to 15 units per mgm. in a standard preparation supplied by the Insulin Committee. Preparation of crystalline insulin from pig pancreas was found to be much more difficult than from fish pancreas. The crystals were less uniform, the sulfur content was less, and the yield was smaller. Physiological activity was 20 units per mgm.—C. I. R.

Insulin and carbohydrate tolerance. Joslin, E. P., Ann. Int. Med. **2**: 1001. 1929.

Joslin criticizes the conclusions of Brace, who stated that his five patients lost tolerance under insulin treatment. All of Brace's patients received caloric intake above the need of a healthy adult, which is contrary to the fundamental laws of diabetic dietetics. Joslin has the impression that a diabetic following reasonable rules increases his or her tolerance for carbohydrate. The diabetic of long duration is more apt to die of complications than of coma. In children the diabetic mortality is very low and in patients under 40 years of age it is decreasing.—E. L.

Eosinophilia in insulin therapy. Lawrence, R. D. and O. B. Buckley, Brit. M. J. **1**: 597. 1929.

One of the authors had in 1927 observed a high degree of eosinophilia in a diabetic patient treated with insulin. Twenty insulin treated diabetics were investigated with the result that ten showed an eosinophilia varying between four and twenty per cent. Blood counts on twelve diabetics being treated without insulin as a control revealed no abnormal eosinophilia. They were unable to offer any definite explanation of the finding but suggested three possible ways in which insulin may be responsible: (1) by virtue of its physiological action; (2) as an allergic phenomenon resulting from the protein nature of insulin or from protein impurities in the solution; (3) by reason of the irritative effect on the skin and subcutaneous tissues resulting from the acidity of insulin.—H. C. Shepardson.

Persistent hypoglycemia following diabetes mellitus treated with insulin. Leyton, O., Proc. Roy. Soc. Med. Clin. Sec. **22**: 71. 1929.

The case described occurred in a male child of 5½ years with a family history of diabetes mellitus on the paternal side. Diabetes was discovered in the child and he was placed upon the proper diet with insulin. The dose of the latter had to be increased to 18 units twice daily. Following the development of a cold, hypoglycemia developed. Thereupon the dose of insulin was decreased slowly until 8 units twice daily were given. At this time severe hypoglycemia developed, which for several weeks threatened the patient's life. Insulin was stopped and in the course of time the symptoms of hypoglycemia subsided. It was observed that during the evidences of hypoglycemia glycosuria occurred nevertheless.—I. B.

Adenoma of the Islands of Langerhans with associated hypoglycemia. McClenahan, W. U. and G. W. Norris, Am. J. M. Sc. **177**: 93. 1929.

This is a single case report with four figures. Antemortem studies on the blood sugar showed values varying from 38-42 mgm. At autopsy a nodule 15x7x16 mm. was found on the pancreas. This nodule (adenoma) was found to be composed of island cells. The islands in the remainder of the pancreas were markedly hypertrophied. The authors conclude that there is a definite relationship between such tumors and the observed hypoglycemia.—E. L.

The dietetic treatment of diabetes mellitus. Newburgh, L. H., Ann. Int. Med. **2**: 645. 1929.

When Allen introduced his diet of high protein, high fat and low carbohydrate, it had a glucose value of 150 grams. Now both Allen and Joslin have modified this diet so that it contains only 80 grams of glucose. Marsh and Newburgh advocated a diet of sufficient caloric value using fat as the chief source of energy and restricting both protein and carbohydrate. The protein must be sufficient to maintain nitrogen balance and the carbohydrate must be ample to insure complete combustion of fat. A typical discharge diet after desugarizing the patient was protein 50, fat 220 and carbohydrate 35. This diet has a glucose value of 86 grams and yields 2300 calories. If this diet is prescribed, about four-fifths of the adult patients will not need insulin. The author does not believe there is any evidence proving or disproving the relationship of diet to arteriosclerosis. This vascular disease is not caused by metabolic products of fat.—E. L.

Regulation of carbohydrate metabolism. Excretion of insulin through the kidneys, and its conditioning (Regulation des Kohlehydratstoffwechsels. Ausscheidung des Insulins durch die Nieren und ihre Bedingungen). Partos, A., Arch. f. d. ges. Physiol. **221**: 562. 1929.

Insulin is a normal constituent of human and rabbit urine. It is not detectable in the urine of fasting rabbits; this explains the production of a higher hyperglucemia of longer duration when fasting animals are fed glucose. During hyperglucemia urine contains no insulin; as soon as the blood-sugar commences to fall insulin is found present. Absorption of carbohydrate is the adequate stimulus for insulin production. After a rich carbohydrate meal the amount of glycogen formed in the liver depends on the amount of insulin previously present. In diabetes mellitus and in experimental diabetes (pancreas extirpation) no insulin is present in the urine. In Sandmeyer-diabetes it is possible to stimulate the islets to insulin production by a rich carbohydrate meal.—A. T. C.

A case of diabetes mellitus showing a glycemia without symptoms. Peters, C. A. and I. M. Rabinowitch, Am. J. M. Sc. **178**: 29. 1929.

This single case report concerns a diabetic whose blood-sugar at one time was 26 mgm. without any clinical symptoms of hypoglycemia. Consequently, 10 units insulin were injected and no food given. The blood-sugar was determined before and after fermentation. For six hours there was no glucose whatever in the blood, according to the authors. The investigators state that though hypoglycemia is an important factor in the symptoms produced by insulin overdosage, it is not the only factor involved.—E. L.

Action of insulin on the motility of the gastro-intestinal tract. I. Action on the stomach of normal fasting man. Quigley, J. P., V. Johnson and E. I. Solomon, Am. J. Physiol. **90**: 89. 1929.

Subcutaneous injection of insulin in amounts of 12 to 20 units usually produces in normal human subjects fasting 11 to 44 hours an increase in gastric motility as recorded by the triple balloon method. The essential features of this response are: (a) an increase in gastric tone; (b) type A contractions; (c) a very prolonged hunger period. The gastric hypermotility induced by insulin is not inhibited by smoking, mild nausea, unpleasant emotions, body discomfort, sight or thought of food, extraneous disturbances, swallowing or the presence of indifferent substances or food in the mouth or in the stomach. The gastric motility is inhibited by introduction of dextrose or cane sugar into the duodenum, and also by the subcutaneous injection of atropine or epinephrine. "Insulin sensations," especially hunger, parallel rather closely the degree of gastric activity. Under the experimental conditions described antiperistaltic movements in the stomach were not associated with sensations of nausea.—Authors' Summary.

Fat metabolism in peripheral tissue (Zur Frage des Fettsloffwecheek in den peripheren Geweben). Raab, W., Wien. Arch. f. Inn. Med. **17**: 439. 1929. Abst., J. A. M. A. **93**: 1184.

Using Bang's method, Raab determined in man the total purified petroleum benzine fraction, the neutral fat and the free cholesterol in blood from the capillaries and from the veins. He found that in normal persons (in the morning with the stomach empty) the differences between the blood from the capillaries and the blood from the veins are inconstant. The eating of sugar antagonizes the retention of fat in the tissues, causing a mobilization of fat from the tissues to the blood. Insulin inhibits the mobilization of fat. Pituitary extract produces a constant decrease in the neutral fat content of the blood. In the patients with diabetes mellitus in whom lipemia is absent, the differences between blood from the capillaries and blood from the veins are just as little characteristic as in normal persons; in patients with marked lipemia, on the contrary, the venous blood usually contains a great excess of neutral fat. In cerebral and hypophyseal adiposity the fat content is unchanged. In the hyperlipemia that occurs in diabetes mellitus the free cholesterol is only slightly increased; the hyperlipemia consists chiefly in an increase in the neutral fat.

A case of extensive atrophy of the subcutaneous fat following injections of insulin. Rabinowitch, I. M., Canad. M. A. J. **21**: 67. 1929.

An illustrated case-report showing an extremely marked effect.—A. T. C.

High carbohydrate diets in diabetes mellitus. Richardson, R., Am. J. M. Sc. **177**: 426. 1929.

Due to inability of patients to absorb completely the fat in high fat diets, the author suggests a diet higher in carbohydrate than that proposed by Newburg and Marsh. The carbohydrate was usually doubled with no increase in insulin. The patients felt better and there were no cases which showed an increased blood-sugar.—E. L.

Insulin resistance and bronze diabetes. Root, H. F., New England J. Med. **201**: 201. 1929.

No cases of true diabetes have been reported in which insulin failed to reduce the sugar. A relative resistance to insulin may arise as the result of destructive processes in the pancreas, complicating disease of the other endocrine glands, disturbance to the function of the liver, and abnormal processes in the skin and muscles. An extensive bibliography is included.—J. C. D.

Can one differentiate certain glycosurias from the true diabetic glycosurias? (Besteht gegenwärtig die Möglichkeit, gewisse Glykosurieformen mit Sicherheit von der echt diabetischen zu trennen?) Salen, E. B. and T. Nyren, Acta med. Scandinav. **70**: 330. 1929.

The authors come to the conclusion from their studies that there is but one definite way of differentiating the non-diabetic from the diabetic glyco-

surias, namely, by the means of a glucose tolerance test in which they lay stress on the length of time of the hyperglycemia and pay little or no attention to the height of the curve. Attempts to differentiate between these two glycosurias by means of insulin, they consider as disproven. The renal glycosuria the authors define as follows: "Normal fasting blood-sugar, normal length of postprandial rise after glucose and a lowered threshold."—H. J. J.

Effects of insulin on the endocrine system (L'influence de l'insuline sur le systeme endocrine [note preliminaire]). Schereschevsky and Moguilnitzky, Rev. franç. d'endocrinol. **6**: 456. 1928.

Post mortem examination of six guinea pigs killed by excessive doses of insulin injected subcutaneously showed an increased size of the suprarenals. Hyperemia was present in the respiratory organs and thyroid, ecchymoses in the kidney, hyperemia and ecchymoses in the stomach and intestinal walls, congestion around the islands of Langerhans. The most characteristic changes were in the adrenals where hyperemia and oedema occurred in the medullary and cortical zones. Both zones showed cellular degeneration. The authors conclude that insulin is not a specific excitant of the vagus, and that its antagonism to adrenalin is of a toxic nature.—B. C.

Isolation of tail of pancreas in a diabetic child. de Takats, G. and R. M. Wilder, J. A. M. A. **93**: 606. 1929.

An operation was designed to promote hypertrophy of the islet tissue of the pancreas and thereby increase the insulin output from the gland. This operation was performed on a child with severe diabetes with encouraging results.—Authors' Summary.

The effect of parathyroid hormone and increased calcium metabolism on the growth of tumor tissue. Goerner, A. and B. G. P. Shafiroff, J. Cancer Research, **12**: 294. 1928.

The effect of parathyroid extract on calcium metabolism of normal and tumor-bearing rats was studied. The calcium content of Flexner rat sarcoma was increased but no inhibitory effect due to calcium was obtained. The calcium content of carcinoma number 10 was not increased, there being no difference in growth from the controls.—M. B. G.

Parathyroid tumors and osteitis fibrosa cystica (Uber die Bedeutung der Epihtelkorper-vergrössung bei der Ostitis fibrosa gereralizata Recklinghausen). Gold, E., Mitt a. d. Grenzgeb. d. Med. u. Chir. **41**: 63. 1928.

A case of osteitis fibrosa cystica is described in a female aged 54. A tumor of the right superior parathyroid was removed by operation. Six months later the previously bed-ridden patient was able to walk, showed marked general improvement and a gain in weight of 11 kgm. No change was noted in the bones by Roentgenologic examination. The tumor presented the microscopic appearance of a benign adenomatous hyperplasia of a parathyroid gland. After its extirpation the blood calcium which had previously been elevated as high as 13.1 mgm. per 100 cc. fell to the normal level of 10 mgm. and likewise the urinary calcium which had been twice as great as normal was reduced to a third the normal amount (from 412 to 24 mgm. in 24 hours). The author inclines to the view, previously expressed by Schlangenhaufer, Maresch, Gunther and Mandl, that the hyperplasia of the parathyroid is responsible for skeletal disease and is not a secondary compensatory phenomenon as suggested by Erdheim. In support of this interpretation he advances the improvement in his patient and Mandl's following the extirpation of parathyroid tumors. Other significant data are cited. Seventeen cases of parathyroid tumor were observed at autopsy in a period of 7 years. Thirteen of these were associated with abnormality of the skeleton. In 4 no skeletal disturbance was demonstrated. With a single exception only one parathyroid gland was enlarged. In 6 of the 13 cases the anatomical diagnosis was osteomalacia, in 5 generalized osteitis fibrosa cystica, in 1 osteoporosis, in 1 "osteitis deformans, Paget." The diagnosis in the last case was doubtful. On the other hand, in 40 other cases of Paget's disease examined by Maresch there was no single instance of enlargement of parathyroids.—Russell M. Wilder.

The effects of insulin on parathyroidectomized dogs. Reed, C. I., Am. J. Physiol. **89**: 239. 1929.

Insulin administration to normal and parathyroidectomized dogs not in tetany will increase calcemia and decrease phosphemia. When in tetany, insulin will relieve symptoms, usually completely, and will produce hypophosphemia. Calcemia responds much less regularly than in normal animals, any increase being followed by a decrease. Tetany alters the effect of insulin on calcemia and to a less extent on phosphemia, but does not affect the post-insulin hypoglycemia curve.—Author's Summary.

Idiopathic or hypoparathyroid tetany in children with special reference to certain psychic manifestations. Shannon, W. R., Arch. Pediat. **46**: 346. 1929.

Of the eight cases reported, six responded to parathyroid administration by an amelioration of symptoms and a variable increase in blood calcium. In the remaining two, one of them in a new-born infant, parathyroid extract was not given and calcium determinations were not made. The psychic disturbances noted in this series were present following the convulsions and consisted of mental depression, irrationalism, acute maniac excitation such as screaming, tearing of clothes, fighting with other children and later nightmares and terrors.—M. B. G.

Influence of splenectomy on the testis (Effet de la splénectomie sur la glande génitale male). Kostitch, A. and A. Telebarkovitch, Compt. rend. Soc. de biol. **100**: 54. 1929.

In white mice splenectomy, either before or after puberty, does not cause regressive changes in the testis.—J. C. D.

Splenectomy and ovarian function (Effet de la splénectomie sur la fonction ovarienne [cycle oestrien]). Radossavlyévitch, A. and A. Kostitch, Compt. rend. Soc. de biol. **100**: 56. 1929.

Splenectomy in white mice at the age of 25-35 days, i.e., puberty, usually produces a precocious appearance of the oestrous cycle as judged by vaginal smears.—J. C. D.

Presentation and action of an active thymus gland extract (Darstellung und Wirkung eines aktiven Thymusdrusenextraktes). Nitschke, A., Monatschrt. f. Kinderh. **41**: 128. 1928.

Repeated injections of thymus extract produced typical clinical pictures of tetany in 24 to 48 hours in rabbits. The blood calcium showed low values, 5 to 9 mgm. per 100 cc. with an average of 7 mgm. per 100 cc. The author was able to show the tetany productive action of thymus extract on 30 animals, the majority culminating in death. No such manifestations were obtained in the control animals. Thymus extract also has an influence on the metabolism of inorganic phosphorus, as low inorganic P. values in the serum of his experimental animals were obtained. According to the author, thymus extract contains two secretions, one capable of lowering the calcium content and the other the inorganic phosphorus content of serum.—M. B. G.

The treatment of exudative diathesis by means of thymus radiation (Die Behandlung der exudativen Diathese Mittels Thymus Rontgenbestrahlung). Vas, E., Jahrb. f. Kinderh. **121**: 293. 1928.

The author found in the majority of children under his observation with exudative diathesis an increase in the thymic shadow as against normal controls. In 38 children with eczema, prurigo or urticaria pigmentosa, he inaugurated thymic radiation. He reports good results especially in children where diatetic and other measures were of no avail. In some of the cases, two or even three treatments by irradiation were necessary.—M. B. G.

Studies on the circulation in Basedow's disease and in cardiac neuroses (Kreislaufstudien beim Basedow und bei der Herzneurose). Bansi, H. W., Ztschr. f. klin. Med. **110**: 633. 1929.

This article contains an extensive review of the literature and records, observations on the velocity of the blood stream in Basedow's disease and con-

ditions simulating it. In Basedow's disease and likewise in pre-Basedow's disease the circulation as a whole is arranged uneconomically due to a quicker passage of the blood through the capillaries and an increased venous return to the heart. There is a poor utilization of the oxygen of the blood caused by the uneconomical working of the circulation. The oxygen tension in the venous capillaries was abnormally high in Basedow and pre-Basedow patients, and some of these patients differed from normal individuals by an alteration in the curve of oxygen dissociation, i.e., by having a higher partial pressure of oxygen. The hemoglobin binds the oxygen less closely and as a result gives it up quicker and more easily. The tissues are bathed in fluid with an abnormally high partial pressure of oxygen. The pre-Basedow patients, according to Bansi's observations, are no longer normal in respect to their work ability. In them the quickening of the pulse was associated with an acceleration of the circulation; on the other hand, the blood chemistry, basal metabolism, and usually the work metabolism were normal. This group of individuals, who formerly were grouped with cardiac neurotics, and whom Bergmann classified with those showing stigmata from the vegetative nerves, differ from the psychogenic or neurogenic cardiac neurotics in the fact, that in pre-Basedow's disease demonstrable disturbances of the circulation are found. The cardiac neurosis in general does not have a change in the speed of the circulation, so that the work of the heart is not increased.—W. D. Reid.

Hyperparathyroidism. Barr, D. P., H. A. Bulger and H. H. Dixon, J. A. M. A. **92**: 951. 1929. Abst., A. M. A.

In the literature on osteomalacia, on multiple cystic tumors of bone and on parathyroid tumors, there is a clinical picture, found occasionally under all of these titles, which seems to deserve description as a separate clinical entity. A survey of the literature revealed some remarkable and little emphasized associations: (1) Few cases of proved multiple giant cell tumors of bone have been reported in the literature. (2) It has been found by many observers that osteomalacia is associated with a negative calcium balance and increased excretion of calcium in the urine. (3) The occurrence of calcium stones and distressing urinary symptoms has been frequently reported in cases of osteomalacia. (4) There have been cases of osteomalacia and other bone diseases in which parathyroid tumors or parathyroid hyperplasia was noted at the time of autopsy. (5) A few cases of osteomalacia have been associated with muscular hypotonia and a complete inability to walk. (6) A high calcium content has been found occasionally in cases which were called osteomalacia and which were associated with multiple cystic tumors of bone. (7) Recent work on parathyroid extract has demonstrated the physiologic changes that occur when there is an excess of the parathyroid secretion. These include (a) hypercalcemia; (b) increased urinary output of calcium and negative calcium balance; (c) depletion of calcium in bone, and (d) hypotonicity of muscle. With the assembling of all the evidence, it seems justifiable to introduce the name of hyperparathyroidism and to consider under this heading the various cases as constituting a clinical entity as definite and distinct as parathyroid tetany or exophthalmic goiter. The clinical features probably are: (1) Rarefaction of bone. (2) The occurrence of multiple cystic bone tumors, several of which on pathologic examination have been found to be giant cell sarcomas. (3) Muscular weakness and hypotonia. (4) Abnormal excretion of calcium in the urine and the formation of calcium stones. (5) Abnormally high serum calcium. All of these changes are secondary to, or associated with, a parathyroid hyperplasia or parathyroid tumor.

The blood lactic acid range in exophthalmic goiter at rest and after exercise (Der Blutmilchsaurespiegel beim Morbus Basedow in der Ruhe und Wahrend der Arbeit). Bier, A., Klin. Wchnschr. **8**: 1306. 1929.

The blood lactic acid at rest was studied in 12 cases of Basedow's disease, and after exercise in 2 normal individuals, 2 cases of exophthalmic goiter and one case of myxoedema after operation for hyperthyroidism. Determinations were made according to the Mendel-Goldscheider method which gives the upper limit of normal as 15 mgms. of lactic acid per 100 cc. At rest the acid level in exophthalmic goiter was found to be near or above the upper limit of normal (14 to 22.5 mgms. per 100 cc.). After exercise (stair climbing) the blood lactic acid in the normal cases rose slowly and fell to the normal resting level

within 6 minutes. In the two hyperthyroid cases the rise was much steeper, reached a higher level (37.5 and 40.5 mgms.) and returned to the resting level after a longer interval. In myocardial insufficiency Eppinger has reported high and prolonged lactic acid curves after exercise. Bier points out that the lactic acid rises more slowly in cases with cardiac disease than in cases with hyperthyroidism. After thyroidectomy the lactic acid curve was similar to the curves in the two normal cases. Oxygen consumption was found to be increased in proportion to the increase in blood lactic acid in hyperthyroidism.

—D. P. Foster.

Unusual forms of hypothyroidism: (1) mild myxedema in two sisters; (2) severe menorrhagia due to hypothyroidism; (3) severe metorrhagia due to hypothyroidism; (4) mild myxedema in a patient with constitutional autonomic dysfunction; (5) end result of cretinism after 16 years of continued thyroid treatment. Blumgarten, A. S., M. Clin. N. Amer. **12**: 593. 1928.

Typical hypothyroidism occurs in two forms; adult hypothyroidism or myxedema and infantile myxedema or cretinism. The symptomatology is the same in both, with the exception that disturbances in growth and mental development occur in the infantile form in addition to the cardinal symptoms of the adult form. Although a careful examination of the myxedematous patient will reveal changes in the various systems of the body, the outstanding symptoms are the skin changes, the circulatory symptoms, and the typical mental sluggishness. When, however, the disturbances in other systems dominate the clinical picture, the hypothyroid etiology becomes obscure. The most common chief complaints in most of the atypical forms of myxedema are the following: rheumatoid pains; severe menorrhagia or metrorrhagia; anemia; obesity; a sensation of pressure on top of the head and severe atonic constipation.—I. B.

Treatment of Basedow's disease (Zur therapie des Morbus Basedow). Bonem, P., Schweiz. Med. Wchnschr. **30**: 764. 1929.

Despite the value of thyroidectomy in Basedow's disease, the risks entailed should not be overlooked. Medical measures to control symptomatology include bromides, possibly with valerian and quinine hydrobrom. Arsenic and gynergen are also useful. Digitalis is useless, but strophanthus or convaleria may be employed if such a drug appears indicated. Iodine therapy is a debatable question and generally does more harm than good. These patients do well at an elevated location of about 3000 feet, where the air is cool and rare. The use of insulin to improve carbohydrate tolerance and increase food intake is still a matter of question. The x-ray experiences of the author are favorable.

—I. B.

Reactive hyperthyroidism in calculous pyelitis (Hyperthyroidisme reactionnel par pyelite lithiasique). Bonilla, E. and S. Ferrero Velasco, Rev. franç. d'endocrinol. **6**: 370. 1928.

The authors emphasize the importance of focal infections in cases of hyperthyroidism characterized by continuous low grade hyperthermia. They describe a case absolutely intractable to classic methods of treatment. The persistence of slight fever led to a search for focal infection and the finding of a small renal calculous, with pyelitis. After elimination of this focal infection the hyperthyroidism disappeared. The authors maintain that hyperthermia of the type discussed is a contraindication to surgical treatment for the hyperthyroidism until the focal infection is cleared up.—E. B.

Tuberculosis of the thyroid gland. Budd, S. W. and C. Williams, J. A. M. A. **92**: 1741. 1929. Abst., A. M. A.

The three cases of tuberculosis of the thyroid reported on by the authors had much in common from both the clinical and the pathologic points of view. The patients were all women of approximately the same age (average, 41 years); all complained of soreness and tenderness in the region of the thyroid of a few months' duration; all three had slightly elevated temperatures and accelerated pulse rates; two had lost weight (average 20 pounds); all were nervous, and two had increased basal metabolic rates. No positive signs of other tuberculosis were found in any of them, but one had had bronchitis for several years, and another had the scar of a cervical abscess and a chronic anal

fistula. Pathologically all had the fibrous type of tuberculosis, which is the most unusual manifestation of the disease. The wounds healed in from two to four weeks; all gained weight (average, 10 pounds), and the general symptoms were largely relieved. Their first patient was suspected of having malignant condition until a frozen section clarified the diagnosis. The second patient seemed to have an acute pyogenic infection and operation was delayed. The third case was diagnosed properly prior to operation.

Thyroid and cerebral activity (Thyroide et activite cerebrale). Cardot, H., J. Regnier, D. Santenoise and P. Vare, Rev. franç. d'endocrinol. **7**: 89. 1929.

Researches and clinical experience seem to indicate that some sort of a relationship exists between the activity of the pneumogastric and certain endocrine glands, and the regulation of cerebral activity. In order to test this theory the authors attempted to make parallel studies of the excitability of the pneumogastric center and a motor center of the brain. Using among others the oculo-cardiac reflex as an indicator, functional relations between the pneumogastric and the sigmoid gyrus were demonstrated. The study of the thyroid relation is treated in a later paper.—B. C.

The effects of ingestion of thyroid upon the thymus, testicle and thyroid (Action de l'ingestion de corps thyroids sur le thymus sur le testicule et sur la thyroids). Courrier, R., Rev. franç. d'endocrinol. **6**: 10. 1928.

The writer shows experimentally that when white rats are fed fresh thyroid tissue, there is a recession of the thymus when insufficient food is present for maintenance of body weight, but that there is no recession if the food supply is adequate. He reaches similar conclusions regarding the testicles. The opposite effects reported by others he attributes to malnutrition. His experiments on the effects on the thyroid gland were carried out on dogs and cats. In these experiments ingestion of thyroid produced involution of the thyroid. There is a discussion of the clinical significance of the experiments.—(Corrected Abst.)—B. C.

Myxedema (presumably) confined to the palate and larynx. Dundas-Grant J., Proc. Roy. Soc. Med. Clin. Sec. **22**: 61. 1929.

A woman aged 20 complained of thickness of the voice, soft stridor on inspiration and occasional dysphagia and general debility. Examination revealed a thickening of the soft palate and uvula, and enormous pale infiltration of the epiglottis almost completely concealing the rest of the larynx. White shiny edema of both ary-epiglottic vaults was present and only an occasional glimpse of the exterior part of the right vocal cord was obtainable. A diagnosis of localized myxedema was made, which was confirmed by very good results obtained from thyroid opotherapy.—I. B.

Osteoporosis secondary to hyperthyroidism. Dunlap, H. F. and A. B. Moore, M. Clin. North America, **12**: 1511. 1929.

Hyperthyroidism due either to exophthalmic goiter or to toxic adenoma and the elevation of the basal metabolic rate by administration of thyroid extract or of thyroxin, are associated with increased calcium excretion, i.e., a greater calcium output than intake, hence a negative calcium balance. A similar phenomenon but to a lesser degree occurs with phosphorus. Osteoporosis occurring in hyperthyroidism was studied with the roentgen rays. The condition affects all the bones but when of moderate or slight degree it is most readily discerned in the spongy bones and those with superficial coverings, such as the skull, ribs, and bones of the extremities. In the long bones it is likely to be most apparent in epiphyses and ends of the diaphyses. The loss of calcium varies in degree from mere increase of translucence, so trivial that it may escape notice, to marked and unquestionable rarefaction. The degree of decalcification appeared to be in direct ratio to the severity and duration of the hyperthyroidism. This is substantiated in the five cases recorded in this paper. In the first case the hyperthyroidism, although severe at the time of admission, had not been prolonged; in the second case, hyperfunction of the thyroid gland had existed only a year. In both cases the osteoporosis was only moderate at most. The last three cases exemplify an intense and enduring

hyperthyroidism with a proportionate absorption of calcium, the latter being so pronounced that the question of metastatic malignancy was raised in two of the three cases.—I. B.

Basedow's disease accompanied by vitiligo and paroxysmal tachycardia (Maladie de Basedow, vitiligo et tachycardie paroxystique en evolution combinee). Etienne, G. and Bequain, Rev. franç. d'endocrinol. **6**: 427. 1929.

A case of Basedow's disease is reported in which a symmetrical development of pigment occurred as in Addison's disease. Favorable response to thyroid treatment, with loss of pigment was observed. The author holds that the sympathetic is probably involved either directly or indirectly through the action of the suprarenal or possibly the thyroid hormones.—B. C.

Influence of internal secretions of vertebrates on invertebrates (Zur Frage der Beeinflussung Wirbelloser durch Wirbeltierinkrete). Fleischmann, W., Arch. f. d. ges. Physiol. **221**: 591. 1929.

Review of the literature suggests that parenteral introduction of thyroid preparation has no action on the metamorphosis of insects, whence it may be concluded that such action is only to be expected in animals possessing a thyroid, or at least homologous tissue.—A. T. C.

The use of vitamins A and D and sodium iodide in the pre-operative treatment of Graves' disease. Fraser, R. H. and A. T. Cameron, Canad. M. A. J. **21**: 153. 1929.

A combination of vitamins A and D and sodium iodide produces the same beneficial effect as "vitiodum" and as Lugol's solution in the pre-operative treatment of Graves' disease. Further evidence has been obtained that the mixture of the two vitamins (without some form of iodine) is without action.
—A. T. C.

Thermal cures and the thyroid gland (Cures thermales et glande thyroide. Etat actuel de la question Premieres recherches personelles). Galup, M. J., Rev. franç. d'endocrinol. **7**: 128. 1929.

Improvement under medication with certain thermal waters of cases evidently due to thyroid difficulty leads the author to believe that the results are due to direct effects upon some of the endocrine organs, possibly the thyroid. He does not believe that the results are due to the radio activity of the water.
—B. C.

Injury resulting from radiation in Basedow's disease. Goette, K., Proceedings of the Department of Roentgenology, **39**: Heft 1. 1929. Abst., Arch. Physical Therapy, **10**: 137. 1929.

A consideration of the course of two cases of moderately severe Basedow's disease, which after radiation (¼ Hed., the other twice, 1/10 Hed.) became considerably worse and died with the symptoms of hyperthyroidism. The aggravation of symptoms must be attributed to the radiation. Radiation therapy also as surgery in true Basedow's disease, is not without risk.

Roentgen irradiation in treatment of hyperthyroidism. Groover, T. A., A. C. Christie, E. A. Merritt, F. O. Coe and E. M. McPeak, J. A. M. A. **92**: 1730. 1929. Abst., A. M. A.

A statistical evaluation of roentgen irradiation in the treatment of hyperthyroidism based on 305 cases is made by the authors. In this series there were 26 cases in which a thyroidectomy had previously been performed, without improvement, with incomplete relief, or with recurrence of toxicity. The results of treatment were: cured of hyperthyroidism, 271, 88.85 per cent; improved, twenty-six, 8.52 per cent; unimproved, eight, 2.63 per cent. One of the most reliable criteria for judging progress in cases of hyperthyroidism is the weight curve. The greatest gain in any single case of their series was 80 pounds (36 Kg.). One of the criticisms that has been made with respect to

the irradiation of hyperthyroidism has been the length of time required to gain improvement or to effect a cure. On an average, 6.6 treatments per patient were administered in this series of cases, and generally 2.7 treatments were given before improvement was first noted. As cases are treated at intervals of three weeks, it is apparent that the average duration of treatment was less than five months and the average lapse of time before improvement began was approximately two months. The authors have not been able to determine from their records the average loss of time from work by the patients of this series, but they have every reason to believe that the economic loss from this source has not been greater than with any other adequate method of treatment, and, on the whole, has probably been less. In this series symptoms of hyperthyroidism on an average antedated the beginning of roentgen treatment more than two years. While the facts and figures given do not justify any final conclusion as to the permanence of cure following roentgen therapy, they at least indicate that results in this regard are quite as satisfactory as with any other method. Among the factors which have contributed to failures to cure hyperthyroidism by radiation therapy, are the following: (1) overwhelming toxicity; (2) serious cardiovascular or other visceral changes, and (3) noncooperation on the part of the patient or the attending physician. As twenty-six patients had had previous thyroidectomies without cure the results of roentgen therapy in this group are slightly more favorable than they are for the entire series, but the difference is not sufficient to be regarded as significant. Five deaths have occurred in the group of 271 cases recorded as cured of hyperthyroidism, as follows: organic heart disease, two; cerebral hemorrhage, one; tuberculous laryngitis, one; unknown, but not due to hyperthyroidism, one. Telangiectasis of the skin is a sequel of roentgen therapy that needs always to be kept in mind. It occurred in six cases, mostly in cases in which there was a departure from the standard technic as to dosage.

Creatinuria as a sequel to fractures of bones and the influence of thyroid feeding upon it and upon the creatinuria of post-encephalitic rigidity. Hirst, Marion and C. G. Imrie, Quart. J. Med. **22**: 153. 1928.

The authors summarize from their study of four patients with fractures, that creatinuria occurred after fractures of bones. The administration of thyroid extract increased the output three fold in a case of fracture of the femur. The excretion was most marked at night. The increase in the output of creatinin preceded any change in basal metabolism or any other nitrogenous constituent of the urine. Blood creatinin was not increased and the uric acid showed only a slight rise. The creatinuria of the Parkinsonian rigidity was practically uninfluenced by administration of thyroid extract in amounts which caused a similar increase in total nitrogenous excretion and basal metabolism to that brought about in the case of fracture of the femur. A diuresis was observed in each case as a result of taking thyroid.—R. C. Moehlig.

The question of iodine in the investigation of goiter (Die Jodfrage beim Kropfproblem). Jansen, W. H. and F. Robert, Deutsches Arch. f. klin. Med. **157**: 224. 1927.

This paper discusses the iodine content of the goitrous thyroid and of the blood in goiter patients and their relation to thyroid function and toxicity. The total iodine content is greater in the goitrous thyroid than in the normal thyroid but the relative iodine content is less. Deficiency of iodine containing foods leads to deficiency of blood-iodine and of iodine concentration in the thyroid; this serves as a stimulus to goiter formation. The toxic thyroid usually shows a relatively low iodine concentration, and the Basedowian goiter particularly has a smaller absolute iodine content despite the common presence of an increased blood iodine. The Basedowian goiter may impoverish itself of its hormone by pouring it out in excess into the blood. The iodine concentration of thyroid tissue and the blood iodine content cannot, however, be taken as an index of the degree of thyroid dysfunction, since in many cases of Basedow's disease not only a lower iodine content in the goiter but a normal blood iodine content is found. The quantitative iodine aspect alone, whether in thyroid or blood, is not a reliable indication of the degree of thyroid activity. Apparently favorable alteration of the iodine content of thyroid tissue and of the blood by the administration of iodine by no means yields uniform results. While in some instances improvement is noted, in others no effects are ob-

served and in still other instances iodine-Basedow symptoms are produced. It therefore appears that iodine chemistry governs the study of thyroid physiology more from a qualitative than a quantitative aspect.—I. B.

Familial occurrence of congenital myxedema (Familiares Auftreten von Kongenitalem Myxodem). Johannsen, N., Acta paediat. **7**: 179. 1928-29.

Of 5 sisters, 3 showed symptoms of internal secretory disturbances which could be attributed to a hypothyroidism. One came under observation at one year of age but in spite of many years of treatment became idiotic. The second was seen a few months after the appearance of initial symptoms, and placed under treatment with thyroid extract with beneficial results. The third sister died at the age of one year from what was evidently a myxedematous condition. The early symptoms of congenital myxedema are constipation, persistence of a low body temperature and hypertrophy of the tongue.—M. B. G.

Seasonal and geographical variations in the iodine and thyroxine content of the thyroid gland. Kendall, E. C., Tr. A. Am. Physicians, **43**: 143. 1929.

Kendall's results confirm the views of Seidell and Fenger that there is a marked seasonal variation in the iodine content of thyroid glands of beef, sheep and swine. Indeed, there is almost 300% variation in the total iodine content in 100 pounds of hog thyroid. The amount in January and February may approach 14 gm. in each 100 pounds, and the amount in August and September may be as high as 38 gm. The percentage distribution of the iodine containing compounds in the thyroid is affected by geographical distribution and it has been shown by Martin that the iodine content of the thyroid glands of sheep grown in England does not vary with the season. The most important factors are probably the diet, the amount of sunshine, the temperature and the iodine available in food. Also the percentage of total iodine in the form of thyroxine may be greatly influenced by changes which occur after the gland has been removed from the animal. Thyroxine possesses qualitatively all of the activity of the gland. The maximal percentage of the total iodine which can be separated as crystalline thyroxine is not more than 15%. Thyroxine appears to represent an intermediate form of the active constituent. The physiological activity of the thyroid gland appears to be due to active thyroxine.—I. B.

The enlarged thyroid in school children (Zur Frage der groszen Schilddruse bei Schulkindern). Kirsch, O., Klin. Wchnschr. **7**: 2157. 1928.

Based upon a study in Wien, Kirsch agrees with the conclusions reached by Samuelson that the diminution in size of the enlarged thyroid is not dependent on iodine administration but on the improvement in general living conditions, especially in the diet. The best prophylactic agent against goiter is a diet rich in animal protein.—M. B. G.

Studies on thyroxin (Thyroxinstudien). Kornfield, W. and E. Noble, Klin. Wchnschr. **1**: 2377. 1928.

Guinea pig experiments showed that thyroxin is from 100 to 200 times as effectual as dry thyroid extract. The therapeutic dose for a child, 50 cm, sitting height is ¼ mgm. daily and for one 70 cm. S. H. is ½ mgm. The effect of thyroxin as well as that of dry thyroid extract is dependent to a great extent on the diet and general nutritional state of the patient.—M. B. G.

The effect of thyroid on the growing organism (Die Wirkung der Schilddruse auf den Wachsenden Organismus). Lukacs, J., Jahrb. f. Kinderh. **121**: 289. 1928.

Thyroid gland was fed to white rats producing an experimental thyrotoxicosis. It was found that the thyroid feeding did not increase the growth under the optimal growth conditions of the animal but when an individual dose was exceeded, an exacerbation in growth occurred. The bones of such thyrotoxic animals showed an osteoporosis. The relative tolerance to thyroid of young animals could be determined but the tolerance was in no way related to the intensity of the bone changes. The thyrotoxic symptoms were also noted in nursling animals, the thyrotoxicosis being transmitted through the milk of the mothers.—M. B. G.

The influence of the thyroid gland on the action of morphine. Lund, C. C. and E. B. Benedict, New England J. Med. **201**: 345. 1929.

Data on the effect of morphine on the metabolism of four rabbits are presented. Each rabbit was observed in the normal, hyperthyroid, and hypothyroid states. A large dose of morphine caused a drop of about 10% in the metabolism of the normal rabbit. The same dose of morphine caused a drop of 20% in the metabolism of a hypothyroid rabbit. No change was produced by the same dose of morphine on the metabolism of the hyperthyroid rabbit. The rate of metabolism of hypothyroid rabbits after a dose of morphine was extraordinarily constant.—J. C. D.

The body temperature in hyperthyroidism (Contribucion al estudio del conportamiento de la temperatura en el hipertiroidismo). Marañon, G. and E. Bonilla, Med. ibera (No. 534), 113. 1928.

In the various types of hyperthyroidism prolonged low-grade fever is very frequently seen. In a large proportion of cases it is possible to demonstrate the existence of a latent focal infection. In all such cases such foci should be sought for. Lucatello has made the observation that in the hyperthermia of hyperthyroidism the axillary temperature is higher than the rectal. In 17 cases of hyperthyroidism the authors have made comparative studies of axillary and rectal temperatures after a half hour of repose and after 1500 meters of moderate walking. In a considerable number of these cases they also determined the basal metabolism in repose and after exercise. In every case of hyperthermia in repose they have found a focus of latent infection. In two only was the sign of Lucatello confirmed and in those two cases the increase of the axillary temperature was slight. There was no relationship between the temperature in repose and the intensity of the hyperthyroidism as judged by clinical symptoms or basal metabolism. After exercise the temperature of the hyperthyroid subjects increased about as in normal individuals. The temperature curves after exercise in three cases studied did not differ significantly from the normal. The basal metabolism increased always after exercise in varying degrees.—E. B.

Influence of thyroidectomy in the parents on the weight of the thyroid in their offspring (Influence de la thyroïdectomie des parents sur le poids de la thyroïde des descendants).

Histological changes in the glands of animals descended from thyroidectomized parents (Modifications histologiques de la glande thyroïde des animaux nés de parents éthyroïdés). Marza, E. and V. Marza, Compt. rend. Soc. de biol. **101**: 234, 236. 1929.

There is a slight reduction in size and weight of the thyroid glands of new born guinea pigs from thyroidectomized parents. Histologically, the differentiation of the glands is retarded.—J. C. D.

Note on the experimental production of lymphadenoid goiter in rats. McCarrison, R., Brit. M. J. **1**: 5. 1929.

On a diet of American white flour 72 to 80 parts, meat residue 5 to 15, olive oil 8, salt mixture (0.45% potassium iodide) 5, distilled water ad lib., 25% of young rats showed goiters in from 75 to 165 days on post-mortem examination. They occurred more frequently in females. The glands were from 2 to 5 times the normal size. The histological features were those of lymphadenoid goitre. As an unsuitable diet containing sufficient iodine is causal in rats, a similar etiology is likely in man.—Wm. Susman.

Hypothyroidism without myxoedema; its recognition and treatment. McKean, R. M., J. Michigan M. Soc. **28**: 128. 1929.

This classification was given to a group of fifty ambulatory patients on the basis of the close approach of many of their symptoms and signs to those in Kocher's original classification of true myxoedema and a like response to thyroid therapy, yet with a complete absence of the non-pitting oedema so characteristic of that affection. With basal metabolic readings lower in many instances than the myxoedema case, with the frequent occurrence (52%) of a

body weight at or below the normal level, and other factors similarly variant, it seemed to the author that we are dealing with a decidedly common clinical entity differing not so much quantitatively as qualitatively, and suggesting that some different process has gone on in the thyroid gland of such patients than in that of the myxoedemic. The nature of this change and its etiology is undetermined, but chronic infections, particularly of the upper respiratory tract, and possibly the routine use of iodized table salt, seem to play a part. The characteristic symptoms and signs of this group are presented and its treatment outlined.—Author's Abst.

Thyroid deficiency as a cause of poor health. McLester, J. S., M. Clin. North America, **12**: 1357. 1929.

The patients in this group presented disabilities which can best be described merely as "poor health"; not the well defined, easily recognized characteristics of thyroid deficiency of high degree. The salient characteristic is lack of endurance, sometimes called chronic nervous exhaustion,—an inability to resist or endure physical or mental strain. However, there is no impairment of the patient's reasoning powers,—he is merely incapable of consistent mental effort and is lacking in initiative. Numbness and vague pains in arms and legs, occasionally chronic joint pains, frequently constipation and vague digestive disturbances, are complained of. Though occasionally there is puffiness about the eyes, the appearance is not that of typical myxedema. Occasionally, not always, there is obesity. Frequently the muscular development is poor, giving the appearance of flabbiness. Some patients are actually underweight,—victims of undernutrition and lowered metabolism. The patient often looks tired but in conversation may brighten up and for a time show normal interest and enthusiasm. Characteristic symptoms of the circulatory apparatus are slow pulse and low blood pressure, and frequently there is a bottle-shaped heart. Low grade secondary anemia is frequently found,—otherwise there is nothing noteworthy about the blood. The urine often contains albumin. Many of these patients are erroneously believed to have nephritis and are treated for this disease. The basal metabolism is always low and furnishes the final criterion by which the patient is judged. All of the patients in this group have had a basal metabolism of 15% or more below the calculated normal. Often it was minus 20 to minus 30%.—I. B.

On the nature of the iodine reaction in exophthalmic goiter; with particular reference to the effect of iodine late in the course of the disease. Means, J. H., W. I. Thompson and P. K. Thompson, Tr. A. Am. Physicians, **43**: 146. 1929.

Iodine response is observed in any stage of exophthalmic goiter, provided the patient is not already receiving iodine. When iodine is continued beyond the 10-day period indicated the metabolism may remain on a level for a time and then may rise slowly. When iodine is omitted it usually rises abruptly. In other words, although iodine in relatively large doses seems to have the power markedly to modify the intensity of thyrotoxicosis in exophthalmic goiter, the authors have no evidence to show that the drug can alter the natural duration of the disease. In chronic or prolonged exophthalmic goiter the response to iodine is especially illuminating. In a number of instances after years of continuous thyrotoxicosis there occurs just as sharp fluctuations in symptoms and metabolism upon the giving or omitting of iodine as those encountered early in the course of the disease.—I. B.

Congenital syphilis of the thyroid gland. Menninger, W. C., Am. J. Syph. **13**: 164. 1929.

Three autopsied cases of congenital syphilis showing lesions in the thyroid gland and one clinical report of hypothyroidism in a congenital syphilitic girl are reported. Both hypothyroidism and hyperthyroidism occur with congenital syphilis and in some cases are unquestionably a part of the syphilitic process. Hypothyroidism is more frequent and probably results in most cases from the effect of an intrauterine toxin becoming manifest at an early age. Hyperthyroidism is more probably the result of the localization of infectious processes in the gland and usually does not become evident before adolescence. Pathologically the thyroid may be normal, larger or smaller in size. Several

cases of gummatous formation have been reported. Spirochetes may or may not be present.—M. B. G.

Tachycardia and hyperthyroidism; report of 3 cases without evident enlargement of the thyroid gland or exophthalmos. Mohler, H. H., M. Clin. North America, **12**: 975. 1929.

Three cases are reported in which tachycardia was an outstanding symptom due to a toxic thyroid gland without evident enlargement. In two of the three cases the tachycardia was associated with a damaged heart, but with no other evidence of congestive heart failure.—I. B.

The intracutaneous salt-solution test in thyrotoxicosis. Mora, J. M., Am. J. M. Sc. **177**: 219. 1929.

Intracutaneous salt tests (0.2 cc. of 0.85% sodium chloride injected intradermally) were made before and after operation in 42 cases of thyrotoxicosis. The time of disappearance of the wheals varied from 15 to 55 minutes, depending on the degree of thyrotoxicosis. In a normal individual the wheal disappears in 60 minutes or more. After operation the time of disappearance was normal.—E. L.

Standardization of thyroid preparations. Morch, J. R., J. Physiol. **67**: 16. 1929.

A review of methods previously employed and description of a new method based on CO_2 production is given. Experimental conditions were standardized. The proposed unit is the amount by weight of thyroid preparation given by mouth to white mice daily for 3 weeks and calculated per 1000 gm. of mouse, that will cause a 15% increase in CO_2 production. Six different preparations of dried thyroid varied from 10 to 100 units per gram by this test, demonstrating the necessity for standardization.—C. I. R.

The Basedowian neurosis and its relation to a special form of neurosis with paroxysmal tremors (Sobre las neurosis Basedowoides y su relacion con una forma especial de neurosis tremorosa paroxistica). Novoa Santos, R., Progresos de la clínica, **36**: 176. 1928.

It is difficult to establish the line of division between typical exophthalmic goitre and those dystonic vegetative disorders designated as Basedowian neuroses. The author has observed five cases of neurosis with paroxysmal trembling which closely resemble an intense febrile chill. All the subjects during intervals between crises showed dystonic symptoms and three showed symptoms of the Basedowian type except exophthalmos. Two of these latter had moderate tumefaction of the thyroid.—E. B.

The function of the thyroid gland containing adenomatous tissue. Plummer, H. S., Tr. A. Am. Physicians, **43**: 159. 1929.

The conclusions drawn by the author are as follows: (1) diffuse hypertrophy and localized hypertrophy are not, in general, part of the same disease process; (2) exophthalmic goiter and adenomatous goiter with hyperthyroidism are distinct entities; (3) the hyperthyroidism of exophthalmic goiter is caused by hyperfunction of the entire thyroid gland; (4) it is probable that the hyperthyroidism of adenomatous goiter is caused by a localized reaction in the thyroid gland and is only an incident in the course of endemic goiter.—I. B.

The effects of iodine treatment, with and without vitamins, on the basal metabolic rate in exophthalmic goiter. Rabinowitch, I. M., Canad. M. A. J. **21**: 156. 1929.

Thyroids from goitrous patients are not lacking in iodine, and when iodine has been administered large amounts may be found in the thyroid tissue. Lack of iodine would seem to be not the only factor responsible for the clinical signs and symptoms of Graves' disease. Administration of a combination of

vitamins A and D and an iodized fatty acid to 12 patients suffering from Graves' disease produced in each case a marked fall in the basal metabolic rate, the average decrease per day being somewhat greater than that in 12 other patients given Lugol's solution.—A. T. C.

Cardiovascular disease associated with nontoxic goiter. Rose, E., M. Clin. North America, **12**: 1157. 1929.

The incidence of cardiovascular disease is greater in patients with so-called simple or nontoxic enlargement of the thyroid than in the average general population. This applies particularly to the later decades of life in goiter belts. The manner in which such cardiovascular damage may be produced is not known. It would seem possible that goiter not capable of producing the syndrome of hyperthyroidism in the generally accepted sense of the term might nevertheless produce an agent capable of injuring the myocardium and vascular apparatus. A further reason for the energetic treatment of simple goiter is presented and the prophylactic value of surgical removal of thyroid enlargements in adult life is suggested.—I. B.

On the treatment of exophthalmic goiter with antithyroidin. Rud, E., Acta Med. Scandinav. **72**: 274. 1929.

Nine patients with exophthalmic goiter were treated with antithyroidin. With the exception of one case, the treatment lasted 6 to 8 weeks. Five of the patients were treated with antithyreoidin-moebius (Merck), 4 with tablettae antithyreoidinini (State Serum Institute, Copenhagen). During the treatment with antithyroidin, or in immediate connection with, there was not observed any improvement of the objective findings (basal metabolism, etc.) apart from what might naturally be due to the general treatment. This applied to antithyreoidin-moebius as well as to tablettae antithyreoidini.

—Author's Summary.

Cardio-renal syndrome and hypothyroidism. Sainton, P., E. Doumer and P. Veran, Ann. de. méd. **24**: 513. 1928.

The relief of some cases of edema as a result of the administration of thyroid has led certain authors to consider the origin of dropsical syndromes to be extrarenal and to revise the pathogenesis of edema. The authors of the present article cite recent reports of observers who have removed edema by thyroid extract and found it to return on cessation of the medication. During the edematous stage the tests of renal function were practically normal. Also there was present marked hypercholesterinemia and a hypoproteinemia, inducing a diminution of the osmotic pressure in the interior of the capillaries where the osmotic exchanges occur. The history of a woman aged 45 years is reported in considerable detail. Until the age of 38 years she was subject to various disturbances; sudden swooning, attacks of migraine, urticaria of the type known as "Quinck's edema," spontaneous ecchymoses, intermittent albuminuria, amenorrhea following a pregnancy in the course of which attacks of tetany occurred. At the age of 38 years she presented in the hospital a severe picture of chloride, uremic, and hypertensive nephritis with a dilated and insufficient heart, resisting absolutely the customary treatment and suggesting a grave prognosis of early death. The patient left the hospital unrelieved. She found by herself and by accident that thyroid extract remedied her condition. She took it in large dosage and recovered rapidly. She has remained for the past seven years in a satisfactory state of health, only by the influence of thyroid medication. From the first this patient presented very clear signs of hypothyroidism: intellectual apathy, tendency to somnolence, chilliness, constipation with signs of muco-membranous colitis, disturbance of the libido, and even amenorrhea. The tests for renal function showed renal insufficiency. All of the foregoing and the edema disappeared rapidly subsequent to the taking of thyroid extract. More recently the tests for renal function show very slight abnormal findings though the patient is clinically well and using an adequate amount of the thyroid extract. These observers believe that the kidneys have finally incurred some permanent injury. The patient likewise displayed an extreme sensitiveness of her skin to light and purpura during the periods of hypothyroidism. The authors conclude that certain cardio-renal patients are merely hypothyroid individuals whose hearts, as well as the kid-

neys, can regain their functional integrity when edema disappears under thyroid medication.—W. D. Reid.

Difference in effect of feeding goitrous material and normal thyroid to chickens (L'hyperstrumisation chez les Gallinacés, son action differente de l'hyperthyroidisation). Sainton, P. and H. Simmonet, Compt. rend, Soc. de biol. **100:** 550. 1929.

Goitrous material from patients showing no hyperthyroid symptoms was dried in the cold. When this was fed to chickens, the usual changes in plumage which follow thyroid feeding failed to develop. Sufficient iodine was added to the material fed to bring its iodine content up to that of normal thyroid without changing the results.—J. C. D.

The enlarged thyroid in school children (Zur Frage der groszen Schilddruse bei Schulkindern). Samuelson, S., Klin. Wchnschr. **7:** 1567. 1928.

Upon the basis of observations of 109 boys and 201 girls in Breslau the author concludes that the administration of iodine does not influence growth of the thyroid. The improvement in the general well-being which occurred simultaneously with the administration of iodine is due to other conditions, especially that of nutrition.—M. B. G.

Endocrine aspects of scleroderma; report of a case with glandular dysfunction. Seale, E. R., South. M. J. **22:** 885. 1929.

A report with discussion of the case of a girl of 15, who showed improvement under treatment with thyroid and ovarian extract.—J. C. D.

The thyroid and headache at the menopause. Stevens, N. C., New England J. Med. **201:** 168. 1929.

The author concludes that there is a definite symptom complex occurring in women between the ages of forty-five and sixty, which is characterized by headache, fatigue, nervousness, subnormal temperature, dry skin, sensitiveness to cold, and a low normal or subnormal basal metabolic rate. Such patients are benefited by the administration of thyroid extract.—J. C. D.

Effects of thyroid preparations upon the spontaneous contractions of the guinea pig uterus (Einfluss der Schilddrusenpraparate auf die Spontankontraktion des Meerschweinchen-uterus). Toth, A., Endokrinol. **2:** 94. 1928.

Thyroid gland fed over a period of time and in sufficiently large doses increases the spontaneous contractions of the uterus up to as much as 100%, and at the same time changes the type of the curve. Thyroxin injections do not give any such results although definitely increased contractions were observed when the thyroxin was added directly to the Ringer bath. Serum filtrate from injected animals did not give the same curve as that of thyroid fed animals. Attention is called to the similarity of the actions of the ultrafiltrate and hypotonic sodium chloride solution.—B. C.

Hyperthyroidism and castration. Changes in weight of bones and other organs (Hyperthyroïdisme et castration. Modifications pondérales des os et des différente organes). Trifon, Nina, Compt. rend. Soc. de biol. **101:** 615. 1929.

Body weight and weight of bones increased most rapidly in hyperthyroid animals, then in order in spayed animals receiving thyroid feedings, in controls, and in spayed animals. The thyroid gland grew most rapidly in spayed and least rapidly in hyperthyroid animals. The adrenals grew largest in controls, next in spayed, next in hyperthyroid animals, and were smallest in spayed hyperthyroid animals.—J. C. D.

Changes in sedimentation speed of erythrocytes in thyroid diseases (Veränderung der Senkungsgeschwindigkeit roter Blutkörferchen bei Schilddrüsenerkrankungen; vorläufige Mitteilung). Tschernosatonskaya, E. P., Klin. Wchnschr. **8:** 791. 1929. Abst., J. A. M. A. **93:** 246.

Experiments were made on thyroidectomized sheep and rabbits and also on sheep which had received thyroid preparations. The sedimentation speeds

in fifty patients with thyroid disturbances were also determined. All patients with hyperthyroidism showed a considerable increase in the sedimentation speed, while in patients with hypofunction of the thyroid this was decreased. The changes in the sedimentation speed were in direct proportion to the severity of the disease. The author concludes that the determination of the sedimentation speed is valuable for the diagnosis as well as for the prognosis of disturbances of the thyroid. It might also prove helpful to test the effectiveness of thyroid preparations.

The rôle of the thyroid and parathyroid glands in vasomotor reflexes. Vincent, S. and J. H. Thompson, J. Physiol. **66**: 449. 1928.

Cats were thyroparathyroidectomized at least an hour after decerebration. Vasomotor reflexes were recorded before and after the second operation, with no change until about an hour had elapsed, which is regarded as a critical period because of the death at this time of many animals without any preliminary signs. In those subjects that survived the critical period, normal depressor reflex responses were changed to pressor, while normal pressor responses were augmented. This reversal was progressive until a maximum was reached, after which a second crisis occurred, usually about six hours after parathyroidectomy. Characteristic signs of tetany appeared and the blood clotted slowly. Visceral trauma during the maximal period preceding the second crisis induced pressor responses in contrast to the depressor effects normally occurring. Visceral denervation did not affect this response. Calcium salts failed to abolish the vasomotor reversal but parathyroid extract did so. Adrenalectomy simultaneous with thyroparathyroidectomy prevented reversal. When performed later the reversal responses were less marked but not prevented. When decerebration was done after thyroparathyroidectomy but before the onset of tetany, vasomotor responses were irregular, with pressor effects predominating. Death occurred much earlier. It is concluded that the augmented pressor response is due not to depression of vasomotor reflexes but to the liberation of an autocoid in some way related to the adrenals, which is normally inhibited by the parathyroid.—C. I. R.

Heart murmurs and the subfebrile state as common thyrogenic symptoms (Ueber Herzgerausche und Subfebrilität als haufig verkannte thyreogene symptome). Zollikofer, R., Schweiz. med. Wchnschr. **26**: 674. 1929.

Heart murmurs are not necessarily indicative of heart disease. In goiter regions heart murmurs occur more often in goitrous than in goiter-free individuals. Many persons with apparently normal thyroids nevertheless possess structural and functional thyroid changes, thus explaining the incidence of heart murmurs. Goitrous children and the aged are relatively free of heart symptoms. Differentiation between primary heart murmurs and those depending upon thyroid enlargement is essential because of differences in prognosis and treatment. The prognosis in murmurs dependent upon goiter is much more favorable as this condition need not be a deterrent to complete social and economic usefulness. To refuse these persons life insurance may lead to a hypochondriac state. Occasionally, too, there is a slightly increased temperature in these patients. Particular care must be exercised to determine the presence of infectious foci and to differentiate between hyperthyroidism and tuberculosis.—I. B.